

*"...where
angels
fear to
tread."*

Next to the atom bomb and the Kinsey report, cancer seems to be the subject most frequently discussed by the unqualified. In the halls of Congress, in state legislatures, in newspaper columns, and on the radio, heavy and incompetent fingers are pointed at conjured bottlenecks in science's effort to solve the most complex of biological riddles. These harangues have lately taken on a new, consistent, and ominous pattern: "organized medicine" is charged with willfully and maliciously suppressing or ignoring evidence that promises vast benefit to cancer sufferers. If such a charge could be made out to be other than wholly irresponsible, it would follow that "organized medicine" is a good deal better organized than it has been in the past, when it failed to suppress insulin, sulfa drugs, penicillin, cortisone, and an impressive list of other therapeutic agents. But perhaps "organized medicine" is interested in hampering only the development of more effective cancer treatment; if so—it has fallen down badly in having permitted nitrogen mustard, folic acid antagonists, triethylenephosphoramide, sex hormones, and a half dozen radiosotopes to find a place in modern cancer therapeutics, not to mention its negligence in curbing recent surgical advances and the development of more

powerful radiations that are providing increased life and comfort to cancer victims.

Of course, a distinction must be made between serious, orderly, and impartial inquiries into what can be done to accelerate control over the major health problems facing our people, such as that being conducted by the House Interstate and Foreign Commerce (Wolverton) Committee, and the intemperate invective of those with axes to grind. For it just so happens that, without exception, the accusations hurled at "organized medicine" come from protagonists of cancer treatments that have failed of recognition and respect. And why have they failed? Because of collusion, conspiracy, callousness, ignorance, or fear that income from surgery will suffer? No—the reason is so simple that we blush to give it: it is because the vast majority of doctors TODAY can tell an effective treatment from a worthless one. The editors of 220 medical journals in this country stand ready to publish anything that in their long experience and expert judgment deserves attention. County and state medical societies, specialty groups, and numerous national professional assemblies together provide literally thousands of forums each year for the specific purpose of permitting those with something worth saying to say it. Yet certain cancer-cure promoters can't get a break.

Their indignant protagonists choose to overlook one fact: a perfectly sound, honest, and effective mechanism exists for evaluating every new therapeutic discovery and claim. It is working in every medical publication and in every medical meeting. In its simplest terms, it is trial by one's peers—a fundamental democratic operation. And it works.

'taint quaint

The cover reproduces a page of a popular Almanac published in the United States in 1803. Its yellowed pages, colonial typography, and preoccupation with the Zodiac have a charming quaintness. But there's nothing quaint about its reference to useless cancer cures. They are as flourishing today as they were 150 years ago.

NEWSLETTER

MARCH, 1954

One of the most intriguing of current experimental treatment efforts is "combination chemotherapy"--the old one-two. The general idea behind combination chemotherapy is to use a second agent to knock out cancer cells that resist the first--or a third to kill those that may survive the first and second.

There are many refinements of logic to this general idea, and they vary from laboratory to laboratory. But most of the researchers have one goal in mind--the complete conquest of an original cancer and all its metastases.

Some of the thinking stems from observations by Skipper (Southern Research Institute, Birmingham), Burchenal (Memorial, New York) and Law (National Cancer Institute) that a few agents have almost completely destroyed animal cancers. The almost was the rub. In each case, the few surviving cancer crumbs took root, developed into sizable tumors, established colonies throughout the system, and killed the once almost-cured host.

A growing group of investigators have been concentrating not so much on reducing tumor mass--which now can be accomplished with many drugs--but on destroying the few recalcitrant cells that sometimes thrive on the very poisons that wipe out all other malignant units. They are seeking the glass jaw, the soft underbelly, the sucker instinct of cells that have no Achilles' heel.

A mounting mass of basic research indicates that this quest has a firm basis in logic. The success of Hauschka (Institute for Cancer Research, Philadelphia) and others in producing tumors with single-cell inoculations and observations that the unstable cancer cell assumes all sorts of forms (with regard to chromosome counts) as it multiplies confirm again the finding that a tumor is made up of a considerable variety of cells. Weinhouse (of the same institute) has supplied two broad general targets for simultaneous chemical attack in determining the relative rates of fermentative and oxidative types of metabolism in the cancer cells. Potter (Wisconsin) has produced a series of potential road blocks that can be applied simultaneously to a single metabolic system. And Colowick and Kaplan (Johns Hopkins) have devised not only poisonous analogues

but, as a second Sunday punch, the metabolic products of the analogues to place gluttonous and careless cancer cells in double jeopardy.

Skipper has reported doubling and tripling the lifespan of leukemic mice with two sequential blocking agents. One of them was amethopterin, the false vitamin that stymies the metabolism of formate into amino acids and sugars and that is a fair antileukemic drug when used alone. The other was ethionine, which closely resembles the amino acid, methionine, and which, by itself, has no antileukemic activity. However, when both drugs were given together, their action against leukemia was prompt and dramatic. When the two agents were given separately—one on one day, the other the next—the results were not better than that wrought by amethopterin alone.

Shapiro and others (Columbia U. Coll. Phys. & Surg.) have produced one of the most detailed of all sequential blocking conspiracies against cancer. The plan calls for determining the relative chemical deficiencies of the tumor. In a general but variable way, tumors are in relatively short supply of such vital cellular commodities as biotin, thiamine, riboflavin, pyridoxine, and catalase. Surrounding normal tissues may have anywhere from two to twenty times as much of some of these items as do the tumors. Shapiro's plan is to create a general shortage of the vitamins and enzymes most lacking in tumor tissues in the expectation that the well-supplied normal cells will survive the shortage, while the already impoverished cancer cells perish. The shortage or shortages would be created by flooding the system with analogues of the scarce commodities.

Some might speculate that normal cells have a lot of this enzyme or that vitamin because they need and use a lot of it. And tumor cells might have little because they don't need much. Some might even conclude that, in the light of their lean metabolic economy, tumor cells can withstand shortages and analogues better than normal cells. But Shapiro's first results belie such reasoning. And so do theoretical and experimental observations elsewhere. A B₆ analogue, desoxypyridoxine, reduced growth of a mouse mammary tumor (low in B₆) to 75 per cent that of untreated controls; a guanine antagonist, 8-azaguanine, reduced it to 15 per cent; and both analogues used together cut the growth rate down to 5 per cent.

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Keeping up

Radioactive Gold in Malignant Effusions

Experience in attempting to control the reaccumulation of malignant exudates in the abdominal and thoracic cavities by radioactive gold (Au^{198}) colloid is recorded. Au^{198} is administered by means of funnel and tubing. After the injection, the wound is sealed with collodion and gauze, and the patient is rotated, first on one side, then on the other, then head down, and then on his face, so as to distribute the radioactive fluid as uniformly as possible throughout the cavity. These turning maneuvers are continued at intervals in the ward for the next two hours. Later on the same day, a physical survey of the patient is made with a Geiger counter, and the distribution of radioactivity is charted. There is always the possibility of finding a "hot spot," owing to loculated fluid, that might lead to dangerously high local dosage; in this case, it might be judged advisable to withdraw radioactive fluid. Radiation reactions appeared in six of sixteen patients receiving abdominal injections, manifested by abdominal pain with vomiting or diarrhea. In eight of fifteen patients who received the radioactive gold intraperitoneally no worth-while clinical effect was obtained, and five died within a short time. In four of the eight, considerable masses were palpable in pelvis or abdomen. In the seven cases in which a measure of success was achieved, reaccumulation of fluid has been controlled for periods of from two to thirteen months. The author suggests that radioactive gold might be used prophylactically in cases in which malignant cells are accidentally

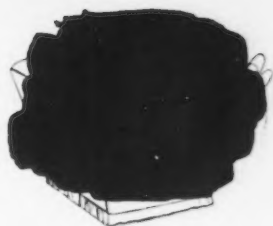
spilled at operation, as in cases of rupture of an ovarian cyst. Au^{198} instilled intraperitoneally at the end of operation, or soon after, might have a decisive effect in eliminating early seedlings.

Walter, J.: Radioactive gold in malignant effusions. Proc. Roy. Soc. Med. 46:466-471, June, 1953.

Differential Diagnosis of Cervical Carcinoma in Situ

There is considerable confusion as to the proper application of the term "carcinoma in situ" and consequent uncertainty as to the management of lesions so designated. This is largely attributable to the fact that the epithelium rarely fulfills all the cytological criteria and the lesions have been seen to regress, or at least not to progress to an invasive state, though untreated. The authors summarize observations on 4152 cervical biopsy specimens obtained between 1930 and 1946. This number included nine invasive carcinomas with previous biopsy specimens, among which one true intraepithelial carcinoma was found. The findings on 4187 cervical biopsy specimens obtained between 1946 and 1952 are presented with particular emphasis on six cases diagnosed "carcinoma in situ" and followed by repeat cervical biopsies without treatment other than the repeat biopsies, which, to date, showed the lesions to be reversible. The desirability of a policy of watchful waiting in the doubtful case, particularly if the patient is young, and the comparative safety of such a policy are stressed. Findings among more than eight thousand cervical biopsy specimens support the conservative point of view that main-

with Cancer



tains that true intraepithelial carcinoma is an exceptional finding with the limited diagnostic facilities at our disposal today. It is hoped that future research will make it possible to recognize beginning cervical carcinoma with certainty and to distinguish it from the benign carcinomimetic lesions that are responsible for the existing confusion in our thinking.

Hoffman, J.; Farrell, D. M., and Hahn, G. A.: Cervical carcinoma in situ: difficulties in differential diagnosis. Am. J. Obst. & Gynec. 66:354-369, Aug., 1953.

Benign Tumors of the Stomach

Benign gastric tumors are divisible into epithelial and nonepithelial polyps. Such a classification is useful in that it coincides with the different clinical pictures and other features found by investigation. The nonepithelial tumor usually encroaches on the gastric cavity and presents a rounded mass of a size that is usually quite apparent roentgenologically; in addition, it often develops an ulcer crater on its summit. The symptoms consist of dyspepsia, abdominal pain, antral obstruction, and repeated or gross hemorrhage. The patients are often seen in a collapsed state, as emergencies. The patients with epithelial neoplasms, on the other hand, have no special pattern of symptoms. Epithelial tumors are usually small and may be multiple; a proportion are malignant or eventually become malignant. Occasionally they bleed severely; they do not form large open ulcer craters on their summits. The author presents four cases of tumors of nonepithelial origin, consisting of one lipoma, two leiomyomas, and one pancreatic-rest tu-

mor. Three of the patients presented histories of digestive disturbance over a variable period of from three weeks to fourteen years. Certain factors affecting the tumor are likely to influence the development of symptoms, namely: proximity of the tumor to an orifice, torsion of pedicle, ulceration and hemorrhage of growth, infection of the ulcer, malignant change, and neuromuscular disturbance. The value of roentgenography in the diagnosis of benign nonepithelial gastric tumors is considerable; the presence of the tumor is usually shown and its benign nature is often evident. Characteristic ulceration frequently occurs in the nonepithelial group and the general picture is so different from that of the epithelial type that it should be possible, in a large proportion of cases, to make the differential diagnosis.

Roberts, R. I.: Benign tumors of the stomach. Brit. J. Radiol. 26:3-12, Jan., 1953.

Granulomatous Prostatitis

Study of the histories in thirty-six random cases of granulomatous prostatitis seen at the Mayo Clinic between 1943 and 1949 reveals nothing specific in the history, course, or physical examination that will distinguish the granulomatous disease. Twenty patients had been diagnosed preoperatively as having carcinoma and sixteen as having benign hyperplasia. Knowledge of a fever or febrile episodes immediately before the onset of urinary symptoms might aid the physician in avoiding an erroneous diagnosis of cancer. However, infection can also appear in a gland already carcinomatous, especially

after catheterization. Caution must be exercised in planning therapy for these patients. Hormonal therapy, such as the administration of stilbestrol or, especially, surgical castration must not be considered without biopsy proof or roentgenological evidence of carcinoma of the prostate. The response to transurethral resection is good in the majority of cases.

Thompson, G. J., and Albers, D. D.: *Granulomatous prostatitis: a condition which clinically may be confused with carcinoma of prostate.* J. Urol. 69:530-538, April, 1953.

Malignant Cutaneous Melanoma

A follow-up investigation of all cases of malignant melanoma, treated in patients in three large teaching hospitals in Glasgow during the twelve years, 1939 to 1949, was carried out in an attempt to establish a basis for planning treatment on anticipated prognosis. The total number of cases of malignant cutaneous melanoma was 132; forty-six patients were still alive, and forty-two of these were seen and examined. The diagnosis was proved by pre- or postmortem histological examination in 128 cases. The variations in treatment applied were so wide that a precise evaluation of methods was impossible. In general, the more peripheral the lesion the better the prognosis; lesions of the head and neck, trunk, and perineum were unfavorable. A statistical survey of the survival rates showed that the prognosis was more favorable in females less than 50 years old, while the prognosis for older women and males of all ages showed little difference. The five-year-survival rate of females less than 50 was 74 per cent. Forty-one per cent of the patients survived five years despite the fact that in many the initial treatment fell short of radical standards.

Wright, R. B.; Clark, D. H., and Milne, J. A.: *Malignant cutaneous melanoma: a review.* Brit. J. Surg. 40:360-368, Jan., 1953.

Surgical Treatment of Gastric Lesions

The surgical methods utilized today in the treatment of gastric malignant neoplasms consist of three basic types: distal

subtotal gastrectomy, proximal subtotal gastrectomy, and total gastrectomy. Encompassing a study of 283 patients operated upon during the fifteen-year period, 1937 to 1951, the survival rates of 161 patients treated by subtotal gastrectomy are compared with those of twenty-four patients treated by total gastrectomy. The over-all operative mortality was 11.9 per cent. The marked decrease in operative mortality during the past four years is attributed to more thorough preoperative preparation and postoperative care, better anesthesia, the use of antibiotics, and increasing experience on the part of the surgeon. The presence of local extension to neighboring viscera and to regional nodes was regarded as of great importance in establishing a poor prognosis for late survival. The authors conclude that the biological behavior of the growth itself and the response of the host are more important in affecting long-term survival than is increasing the scope of gastric resection. Total gastrectomy is recommended for large primary lesions without lymph-node or distant spread. Because of these statistical results and the growing dissatisfaction with the mechanical and physiological aspects of total gastrectomy, the authors suggest that subtotal gastrectomy may be the procedure of choice for malignant lesions in the distal portion of the stomach.

Kirschner, P. A., and Garlock, J. H.: *An appraisal of surgical treatment of gastric malignancy.* Ann. Surg. 138:1-6, July, 1953.

Hormone-Producing Ovarian Tumors

This study of a large number of hormone-producing ovarian tumors, including material from the Ovarian Tumor Registry, is concerned chiefly with the pathology and histology of the masculinizing and feminizing types of tumor. In the former category are included the masculinoblastomas, arrhenoblastomas, the adrenal tumors, and the hilus-cell tumors. The histogenesis of the masculinizing type of tumor is still controversial. The characteristic syndrome of these tumors comprises a group of symptoms indicative of

defeminization followed by an array of positive masculinizing symptoms. The feminizing group includes granulosa-cell tumors and thecomas, which are derived from the feminine mesenchyme. The clinical effects of these estrogen-producing tumors depend upon the age at which they appear—prepubertal, during reproductive life, or postmenopausally. This group of tumors is not infrequently associated with endometrial carcinoma and, while less malignant than carcinoma of the ovary, the granulosa-cell tumor has a high incidence of recurrence. The author attempts to establish a satisfactory working classification of these tumors that is based on an appreciation of existing inadequacies and the reasonable certainty that future advances will necessitate changes in our concepts of the histogenesis and biological implications of these tumor groups.

Novak, E.: *Hormone-producing ovarian tumors. Obst. & Gynec. 1:3-14, Jan., 1953.*

Surgical Treatment of Cervical Carcinoma

An analysis of the results obtained with surgical treatment of carcinoma of the cervix in 100 women is presented. The first patient was operated on in 1939 and the last in 1948 all having had stage-I or -2 carcinoma. The series was slow to accumulate because the author selected good operative risks, fairly young and not too fat. With increasing experience, nearly all patients with cervical cancer are now considered operable, but surgical treatment of the advanced cases is experimental. The occurrence of ureteral, bladder, and bowel difficulties constitutes the greatest drawback to operation and in this series only those were considered who could be operated on without the removal of bladder or rectum. It is felt that roentgen-ray and radium radiation is still the proper treatment for carcinoma of the cervix. Evaluation of the results with regard to the grades of malignancy revealed that they were very satisfactory in Gr. I, but (strangely enough) better in Gr. IV than in Gr. III, and in Gr. III than in Gr. II. Twenty-five patients died, five of inter-

current disease with no record of recurrence. In seventeen of the fatalities the lymph nodes were involved. This study suggests that heavy doses of radiation are not necessary to cure localized carcinoma and that lymph-node lesions will not be destroyed by irradiation. The importance of a check of "cured" cases by the pathologist is emphasized, because the cure rate of cancer in situ is nearly 100 per cent, and such cases should not figure in an evaluation of a therapeutic method.

Meigs, J. V.: *Carcinoma of the cervix—an experience with the surgical treatment. Ann. Surg. 137:660-672; disc. 672-673, May, 1953.*

Treatment of Carcinoma of the Prostate

In the past seventeen months, the authors treated 120 cases of inoperable carcinoma of the prostate with radioactive gold. All possible operative procedures are carried out before the injection of the gold is begun. About 98 per cent of the patients treated showed rapid decrease in the size of the palpable neoplasm. Eleven of thirty-seven cases with postinjection biopsies showed no evidence of neoplasm. Of the fifty patients described in detail and observed from six to seventeen months, twenty-seven are alive without evidence of carcinoma. Eight are alive with clinical evidence of the disease, and eight died with the disease. Complications are almost exclusively confined to rectal irritation. There were fifteen cases in the first fifty, and three in the subsequent sixty-seven, with this complication. Four developed rectal ulcers, three of which required colostomy.

Kerr, H. D.; Flocks, R. H.; Elkins, H. B., and Culp, D.: *The treatment of moderately advanced carcinoma of the prostate with radioactive gold. Am. J. Roentgenol. 69:969-977, June, 1953.*

Carcinoma of the Urinary Bladder

An evaluation of cancer of the bladder from the standpoint of therapy and prognosis is presented, and an attempt made to correlate clinical grading, microscopic grading, and histological classification with the treatment and prognosis in

ninety-six consecutive cases of malignant neoplasms of the bladder. As might be expected, the cases classified as clinical grade-1 or -2 transitional-cell carcinoma with well-differentiated histological features have a better prognosis than those of the same clinical grades with microscopic Grade-III or -IV classification. The clinical grade-3 and -4 groups have a guarded prognosis regardless of the histological grading of the neoplasm. Treatment is summarized as follows: for clinical grade-1 tumors—transurethral resection and fulguration, with good results; for clinical grade-2 tumors—transurethral resection and fulguration, suprapubic cystotomy, and partial cystectomy, with moderate success. Clinical grade-3 tumors were treated satisfactorily only occasionally regardless of the methods used, and clinical grade-4 tumors received only palliative therapy with questionable results. In determining the prognosis of cases of transitional-cell carcinoma, the most reliable and applicable criteria are a combination of the clinical grade of the neoplasm and its histological features.

Hejtmancik, J. H., and Childers, J. H.: A clinical and pathological study of carcinoma of the urinary bladder. J. Urol. 69:377-389, March, 1953.

Incidence and Results of Treatment of Myeloid Leukemia

The occurrence of chronic myeloid leukemia is reported in twenty-four men and thirty-two women who were admitted to the Royal Cancer Hospital in London between 1936 and 1951. The average age of onset of the disease for the fifty-six patients was just over 44 years. Comparison with groups of cases of chronic myeloid leukemia reported by other workers suggested a shift toward a higher proportion of females to males. The duration of the disease, whatever treatment was employed, has remained remarkably constant over the last thirty years and is be-

tween three and four years. Roentgen-ray radiation alone or in combination with chemotherapy has been used in most cases. The technique usually adopted consisted of irradiation of the spleen only; the average dose given was between 50 and 1500 r in four to eight weeks, though in some patients a good remission was obtained with a smaller dosage. Comparison of the methods of treatment used showed that better results have been obtained with external roentgen-ray radiation than with other methods so far employed.

Ledlie, E. M.: Chronic myeloid leukaemia. II. A comparative analysis of the incidence and of the results of treatment of 56 cases. Brit. J. Radiol. 26: 290-295, June, 1953.

Cancer as a Chronic Disease

Experiences with a group of seventeen cases of cancer that originated in various organs, including the thyroid gland, neck, breast, orbit, parotid gland, and the kidney, are summarized. These cases were unusual in that the patients had prolonged periods of active, useful life, even though the malignant disease had not been completely eradicated by surgical means. The authors indicate that cancer may behave as a chronic disease for more than a quarter of a century, as there is wide variation in individual resistance of patients to malignant growths, and that chronicity is not confined to any particular type of cancer. In view of the absence of a completely acceptable explanation for the prolonged survival rate of some patients afflicted with cancer, there is need to be cautious in estimating the survival rate of patients when offering a prognosis to patients and their families. Furthermore, prolonged and sometimes unexplainable periods of survival after diagnosis of cancer reveal why some so-called cancer treatments are accorded at least temporary support.

Morton, J. J., Jr., and Morton, J. H.: Cancer as a chronic disease. Ann. Surg. 137:683-703, May, 1953.



a glance . . .

**one-minute abstracts
of the current literature
on cancer . . .**

Smoking and Cancer of the Lung

The question of the existence of an association between smoking and cancer of the respiratory system stimulated the study of retrospective smoking histories of 3081 patients with cancer of the lip, tongue, other parts of the oral cavity (excluding tongue), pharynx, esophagus, larynx, lung, and skin and of 615 patients with illnesses other than cancer. The findings in this study were also compared with those of several other recently reported investigations, and the magnitude of relative risk of lung cancer among smokers and nonsmokers, demonstrated in this study, has been compared to that found in two other studies. In this series, the rate in smokers was estimated to be five times that in nonsmokers, while in the other two studies it was fourteen times. It is concluded that, in this series, the following associations are demonstrated and real: between pipe smoking and cancer of the lip, between cigarette smoking and laryngeal cancer, and between cigarette smoking and cancer of the lung. Although these associations are statistically significant, the question of whether smoking is etiologically related to lung cancer remains. Considerations are presented that lead to

the conclusion that the etiological significance of these associations remains unestablished.

Sadowsky, D. A.; Gilliam, A. G., and Cornfield, J.: The statistical association between smoking and carcinoma of the lung. J. Nat. Cancer Inst. 13:1257-1257; Addendum, 1257-1258, April, 1953.

Bronchial Carcinoma—Treatment

At one large general hospital in London with 800 necropsies a year, bronchial carcinoma accounts for 30 per cent of all carcinomas examined postmortem. Apparently radiotherapy has little effect on survival nor has it any useful place in postoperative treatment of patients. The palliative effect of radiotherapy, on the other hand, is sometimes impressive. It is the only treatment if operation is contraindicated by the presence of metastases, poor respiratory and general condition, tumors in both lungs, a large or bloody pleural effusion, vagal or sympathetic paralysis, and caval or tracheal obstruction. The usual surgical procedure is dissection pneumonectomy. Provided the operation is anatomically possible, it is well worth while. With regard to the patient's condition following pneumonectomy, disablement is slightest in children while young, and middle-aged men can

usually return to any except heavy manual work. Patients who have one lung removed run a serious risk of cor pulmonale and they should undertake only light work.

Anon.: Treatment of bronchial carcinoma. Lancet 2: 613, Sept. 27, 1952.

Early Diagnosis of Bronchogenic Carcinoma

Because of the tremendous increase in the incidence of bronchogenic carcinoma, it is imperative that every physician consider the possibility of this lesion in every man past 40 years of age who has unexplained thoracic discomfort and who has been a heavy cigarette smoker. It is recommended that all men past 40 years of age who have been heavy smokers for a number of years undergo routine chest roentgenography at least every six months and preferably every three months. Then, if a lung cancer does develop, it can be detected at a time when the lesion is still limited to the lung and even before it produces symptoms. The relative merits of the various diagnostic procedures currently employed including roentgenography, bronchoscopy, cytological examination of bronchial aspirations and sputum, thoracoscopy, and aspiration biopsy are discussed. The authors consider thoracic exploration a justifiable method of diagnosis, since in approximately 20 per cent of patients with proved bronchogenic carcinoma a positive diagnosis can not be made before thoracic exploration. If bronchogenic carcinoma is found, immediate pneumonectomy together with removal of all the mediastinal lymph nodes should be performed.

Ochsner, A.; DeCamp, P. T., and Ray, C. J.: The early recognition of bronchogenic carcinoma. J. Am. Geriatrics Soc. 1:250-258, April, 1953.

Lung-Cancer Problem

The lung is the only anatomical site that has shown an increasing incidence of cancer in recent years. Investigations into the various inhalable elements in the environment have begun on the hypothesis

that, in susceptible individuals, the several carcinogens isolated from such sources as industrial, mining, or automotive by-products and cigarette smoke may contribute to induce a neoplasm by chronic irritation. It is not too farfetched a supposition that the effects of the coal tars and arsenic contained in tobacco in conjunction with the relation of the smoke itself could be related to lung-cancer formation. Clinically one finds not infrequently that a patient with carcinoma of the lung has had a "cigarette cough" of many years' duration and that it suddenly has changed character and becomes more productive. The value of exfoliative cytology in obtaining an accurate histological diagnosis and the advances in the understanding of the problems that are involved in exploratory thoracotomy are discussed. In those cases in which surgical resection is not possible and in which palliation must be considered, a more aggressive attitude toward the unresectable lung cancers confined to the thoracic cavity has been adopted. Enlightenment of the public and the profession is emphasized as the most important single aid that can be said to increase the rate of cure for lung cancer.

Cahan, W. G.: Newer trends in the lung cancer problem. J. Am. M. Women's A. 8:259-265; 275, Aug., 1953.

Indeterminate Pulmonary Lesions

The symptomatology of indeterminate pulmonary lesions may vary considerably from lack of clinical manifestations to a host of complaints that may include cough with or without expectoration, pain, hemoptysis, malaise, anorexia, weakness, and loss of weight. Most primary neoplastic lesions of the lung are of the malignant type, only a small percentage being benign in nature. Of the malignant group, the squamous-cell-type tumor represents a larger percentage of the peripheral lung tumors than was formerly suspected. Adenocarcinoma of the lung metastasizes earlier than the squamous-cell type, some of which have been followed for as long as three or more years without exhibiting

metastases. Differentiation of chronic nontuberculous suppurative pneumonitis from pulmonary cancer or tuberculosis may be impossible without histological examination of the tissue removed. Congenital lesions may be of the pulmonary or vascular type. Other conditions that produce shadows on roentgen-ray examination and that may resist recognition include interlobar fluid cysts, mediastinal celomic and bronchial cysts, and other mediastinal tumors. The outlook for pulmonary cancer will be much enhanced if the benefit of early exploration in patients with indeterminate pulmonary lesions is kept in mind.

Adams, W. E.: *Indeterminate pulmonary lesions*. Illinois M. J. 104:205-208, Sept., 1953.

Primary Carcinoma of the Lung

Primary carcinoma of the lung is synonymous with bronchogenic carcinoma, since nearly all primary lung carcinomas arise from undifferentiated stem cells in the basal membrane of bronchi and are predominantly hilar in location. Modes of metastatic spread of primary lung carcinoma are locally through the lungs, to lymph nodes, and to distant organs. The four most common early symptoms: cough, chest pain, dyspnea, and expectoration with or without hemoptysis, are due to bronchial irritation, obstruction, and ulceration. Primary bronchogenic carcinoma must be ruled out regardless of physical findings when such symptoms as an obstructive wheeze, clubbing of fingers, and weight loss occur singly or in any combination in an individual, especially male, more than 40 years of age. Regarding the various diagnostic procedures employed: bronchoscopy is recommended in all questionable or suspicious cases, while cytological examination of sputum and bronchial washings is considered promising in the early detection of the disease. Of the various laboratory tests an elevated erythrocyte sedimentation rate is the most constant finding. The authors conclude that the only hope for cure in primary lung carcinoma is total pneumonectomy with complete re-

section of the bronchial and mediastinal nodes. Although age alone is no contraindication to surgery, certain conditions would definitely preclude any surgical procedure. Since present knowledge of this disease indicates that the best chance for the cure of bronchogenic carcinoma lies in its early discovery, the authors suggest that yearly chest roentgenograms of all persons and routine chest roentgenograms of all hospital admissions should be common medical practice.

Gittens, S. A., and Mihaly, J. P.: *Primary carcinoma of the lung*. Dis. of Chest 21:641-654, June, 1952.

Solitary Pulmonary Metastases in Cervical Carcinoma

Six patients with carcinoma of the cervix who subsequently developed a solitary pulmonary tumor without other evidence of simultaneous distant metastases are described. The pulmonary lesions developed from nine to fifty-four months after irradiation therapy was given for the cervical lesion. The differentiation between a solitary metastasis and a second primary tumor was not possible on the basis of the roentgenographic, gross, and microscopic examinations. As determined by the studies reported, the combination of primary tumors in the lung and cervix seems to be extremely rare. Indirect evidence cited in the paper would seem to indicate that the pulmonary lesions in the patients described probably represent metastases from carcinoma of the cervix. Metastatic tumors can simulate primary lung tumors both clinically and radiographically, and pulmonary metastases are by no means rare in carcinoma of the cervix.

Seaman, W. B., and Arneson, A. N.: *Solitary pulmonary metastases in carcinoma of the cervix*. Obst & Gynec. 1:165-176, Feb., 1953.

Diagnosis of Bronchogenic Carcinoma

Vital statistics throughout the world indicate that there is a rapidly increasing incidence of bronchogenic carcinoma. Confusion in its proper recognition may

be due to the coexistence of benign pulmonary disease or to simulation of a benign pulmonary lesion by the malignant tumor. The usual symptoms of carcinoma—cough, hemoptysis, chest pain, weight loss, dyspnea, and anemia—are also common in the patient with tuberculosis. However, the cough in cancer of the lung, as distinguished from the cough in tuberculosis may increase progressively in frequency and irritation without an increase in sputum. Progressive weight loss and anemia in a patient under proper treatment for tuberculosis should suggest the problem of cancer. The most common cause of delay in detecting bronchogenic carcinoma is the erroneous diagnosis of unresolved pneumonia. This diagnosis should never be regarded as final until every effort has been made to exclude the presence of a neoplasm and until the patient has completely recovered without recurrence. Signs and symptoms of bronchiectasis may obscure the presence of neoplasm. Exploratory thoracotomy is frequently necessary to establish with certainty the diagnosis of benign lesions, including dermoid cysts and teratomas, especially those occurring near the hilum.

Brindley, G. V., Jr.: *Bronchogenic carcinoma simulating benign pulmonary disease. Ann. Surg.* 137: 616-624; disc. 625-627, May, 1953.

Metastasizing Bronchial Adenomas

A complete review of the literature plus a study of some 111 cases from the Mayo Clinic revealed eighty-seven cases in which a bronchial adenoma had metastasized either distantly or to lymph nodes. Extension directly to adjacent lung tissue, bronchi, or vessels was not included as metastasis. Results of the study demonstrated that the incidence of metastasis of this tumor is nearly 10 per cent. Although the cylindroma type of adenoma occurs much less frequently than the carcinoid type, it is apparently three times as likely to metastasize. Sites of metastasis were, in

order of frequency: lymph nodes, liver, opposite lung, ipsilateral lung, pleura, esophagus and other mediastinal structures, and miscellaneous organs including the brain, kidney, and adrenal. Prognostically, when lymph nodes only are involved, particularly by direct extension, the prognosis is relatively good. When distant metastasis has occurred, prognosis is poor but survival may be prolonged for many months or even years. Except under special circumstances, patients with bronchial adenoma are best treated by appropriate pulmonary resection.

McBurney, R. P.; Kirklin, J. W., and Woolner, L. B.: *Metastasizing bronchial adenomas. Surg., Gynec. & Obst.* 96:482-492, Apr., 1953.

Solitary Circumscribed Lesions of the Lung

A review of 156 cases of solitary circumscribed lesions of the lung obtained from the files of the Mayo Clinic during the period January, 1940, through June, 1951, is presented. All cases in which complete surgical removal of the solitary circumscribed lesions was performed without regard to size, preoperative diagnosis, or presence of respiratory symptoms constituted the basis of this study. Cases were selected solely on the basis of roentgenographic appearance of the lesion. Approximately 35 per cent of the lesions were malignant and 65 per cent were benign. All lesions in which calcification was roentgenographically demonstrated indicated benignancy. An evaluation of various diagnostic procedures is attempted and the cytological examination of sputum was the one laboratory test of absolute diagnostic value. It is concluded that with few exceptions the finding of a noncalcified solitary pulmonary mass constitutes an indication for exploratory thoracotomy.

Hood, R. T., Jr.; Good, C. A.; Clagett, O. T., and McDonald, J. R.: *Solitary circumscribed lesions of the lung; study of 156 cases in which resection was performed. J.A.M.A.* 152: 1185-1191, July 25, 1953.

The Place of Tobacco in Lung-Cancer Etiology

Ernest L. Wynder, M.D.

Clinical and statistical investigations continue to show a definite association between cancer of the lung and smoking. Twelve different and independent investigations covering more than 4500 lung cancer patients have now been conducted in five different countries and the conclusion has been reached that the risk of developing lung cancer increases with the amount smoked.

The statistical association has gained considerably in etiological significance because the tobacco data are compatible with the existing incidence data on lung cancer. The great rise in lung cancer is compatible with the increased tobacco consumption. The tobacco data are compatible with the present predominant male ratio on the basis of the long-term habits of the two sexes; they are compatible with the fact that lung cancer occurs most commonly in cities where smoking habits, particularly that of cigarette smoking, are more extensive than in rural areas. They are also compatible with the fact that cancer of the lung is most pronounced in the younger age groups that have more extensive smoking habits than the older age groups. Thus, because the results of the clinical studies fit in with these different phases of lung-cancer incidence, considerably greater importance is given to tobacco as a causative factor in lung cancer.

While cigarette smoking is most markedly associated with lung cancer, a positive association is also found with cigar and pipe smoking. The reasons for the different degree of association are currently being investigated. At present it seems likely that the greater practice of inhalation among cigarette smokers accounts for the greater association with lung cancer among cigarette smokers.

While certain occupations are asso-

ciated with greater susceptibility to lung cancer, the occupational data cannot account for the great increase in lung cancer. City smoke, while containing known carcinogenic elements, also cannot account for the range of incidence data, particularly in regard to the sex difference.

Large-scale experimental studies in various laboratories in the United States are now being carried out to identify the suspected carcinogen(s) in tobacco tar. The presence of such agents seems well established on the basis of recent experiments by Wynder, Graham, and Cróninger of Washington University in St. Louis, Missouri, in which 44 per cent of eighty-one mice painted with cigarette tar, prepared in a manner closely simulating human smoking habits, developed histologically proved epidermoid cancer upon application of the material to the skin. So far no known carcinogens in tobacco tar have been identified. It is suspected that the identification will bring forth an agent or agents as yet unknown as a carcinogen in cancer research. These studies are now being carried out on a broad front in combined chemical and biological investigation.

Two steps could be taken that should lead toward the prevention of lung cancer: 1. Moderation of smoking habits; this measure seems advisable in as much as it has been established that the risk of developing lung cancer increases with the amount of tobacco smoked. 2. Reduction or removal of carcinogens from tobacco; removal of possible carcinogenic agents from tobacco might be the most far-reaching preventive measure if practical and possible. It is along these lines that much research is being directed now, a research

From Memorial Center for Cancer and Allied Diseases, New York, New York. Abstract of the paper read before the Scientific Session, Annual Meeting, American Cancer Society, Inc., November 3, 1953.

in which the public, physicians, and tobacco manufacturers should have the utmost interest and place their greatest co-operative efforts.

No data available at present provide any information on the usefulness of cigarette filters. Extensive work is required on this subject.

In view of the great and ever-increasing incidence of lung cancer and its great mortality, preventive measures seem to be the most important. It is realized, of course, that tobacco is just one of the factors in the development of lung cancer. There are also the factors of internal predisposition, about which we know very little today; there are a few other exogenous fac-

tors. But the massive clinical evidence, coupled with known incidence data, shows tobacco to be one of the most important factors in the production of lung cancer.

It is a factor concerning the vast majority of lung-cancer patients, and above all, it is a factor that we can understand today and learn to understand more in future experiments. In preventive medicine we must first tackle those factors that are known to us at present. Many diseases in the history of medicine have been virtually eliminated by preventive measures before every detail or mechanism of the disease was understood. Our greatest hope against lung cancer lies along the line of prevention—a hope that shall be realized.

Excerpts from Recommendations Adopted by the Symposium on the Epidemiology of Cancer of the Lung, Louvain, July 12-24, 1952.

Each case of cancer of the lung is to be classified anatomically in accordance with the "International Statistical Classification of Diseases, Injuries and Causes of Death," 1952.

The following methods are available for establishing the diagnosis of primary cancer of the lung: 1. Case history and physical examination. 2. Radiological examination. 3. Bronchoscopic examination without biopsy. 4. Cytological examination of sputum and bronchial aspirates. 5. Cytological examination of pleural fluid. 6. Histological examination of metastases. 7. Histological examination of the primary tumor. 8. Necropsy examination.

A significant part of the progressive increase in number of cases and deaths ascribed to cancer of the lung is absolute, and further research as to the extent of this increase should be undertaken.

Among the considered possibilities with regard to etiological factors were: 1. Smoking of tobacco; there is now evidence of an association between cigarette smoking and cancer of the lung, proportional to the total consumption. 2. Atmospheric pollution from effluvia and smoke from factories and domestic fires and from exhaust fumes from gas and Diesel engines. 3. Occupational hazards, particularly in handling asbestos, chromates, nickel compounds, and radioactive substances. 4. Other environmental factors, as intratracheal injections, skin painting and cubcutaneous injections of carcinogens, tissue transplants, and material deposited in the nose and oropharynx. 5. Variations in susceptibility. 6. Coaction of etiological factors. All these factors require further international, co-operative, and correlated study.

Anon.: Symposium on the epidemiology of cancer of the lung. Acta, Union internat. contre cancer 9:437-636, 1953; pp. 441-446.

The Place of Tobacco in the Etiology of Lung Cancer

E. Cuyler Hammond, Sc.D.

Personally, I find the problem of trying to determine the causes of the tremendous rise in lung cancer a fascinating problem particularly from the standpoint of scientific methodology; but with more than 20,000 Americans dying of this disease in the last year and the toll continuing to mount, it is a deadly serious matter. The public has put its trust in scientific investigators not only to find the technical answers but also to suggest a practical solution. Therefore, we as scientists have a moral responsibility to view the problem in all its aspects and implications rather than merely from within the narrow confines of our specialty. For this reason, I would like to start by discussing some general considerations.

Once we obtain the impression that a certain factor is primarily responsible for the increase in lung cancer, how sure must we be of the facts before we as scientists urge the public to take action accordingly? The moral issue here is similar to that which arises when a new drug has first been tested on a few experimental animals with promising results. We must weight the possible good against the possible harm, bearing in mind the alternatives. For example, one of the dangers of the premature general use of a new treatment is that it may deprive patients of the benefit of the standard moderately effective methods already in use or of alternative new methods.

From what we know at present, there are at least three different environmental factors and probably more that could be at least partly responsible for the rise in lung cancer: (1) cigarette smoking; (2) exhaust fumes from automobiles; and (3) air pollution from coal and oil furnaces. All of these contain substances that can produce tumors in experimental animals. All three come into direct contact with

the lung. All three affect a very large proportion of the population. The first two, and to some extent the third, have been increasing during the period in which lung-cancer death rates have been rising. The last two, automobile fumes and general air pollution, are heaviest in urban areas, and reported death rates from lung cancer are higher in urban areas than in rural areas. Whether cigarette smoking is also heavier in urban areas than in rural areas in the United States is somewhat uncertain, but this will be known before long. Wynder said it is so in England.

In my opinion, the full facts are not yet known about any of these possible factors. Some investigators have expressed the opinion that, while cigarette smoking may not be the only cause of lung cancer, it is at least by far the most important cause and accounts for the increase in the death rate. If this view is now accepted as fact, it inevitably will have the result of reducing research in respect to other possible causes. After all, you cannot expect the public to put up millions of dollars for investigation of other possibilities if everyone thinks the answer has been found. For this reason, if for no other, I should want very strong proof indeed before I would be willing to state as an absolute fact that I know cigarettes to be responsible.

There are two quite separate and distinct aspects to the problem of smoking in relation to lung cancer: (1) the abstract, scientific aspect; and (2) the applied, practical aspect.

On the scientific side, we have first to answer a simple, direct question: Does smoking increase the probability that an individual will develop lung cancer? If the answer is in the affirmative, the most

Presented at the Scientific Session, Annual Meeting, American Cancer Society, Inc., November 3, 1953.

important question then becomes: How great is the effect of smoking on the probability of developing lung cancer? The second question is considerably more difficult than the first to answer accurately.

Evidence bearing on the problem has come from three sources: (1) morbidity and mortality trends in relation to trends in smoking habits, (2) laboratory experimentation, and (3) a number of studies in which lung-cancer patients and control individuals were questioned as to their past and present smoking habits.

The death rate from lung cancer, particularly among males, has been increasing dramatically during the last several decades and the sale of cigarettes has had a parallel increase. This is circumstantial evidence of a type that should lead to suspicion but not to conviction unless more direct evidence is presented. It does, as it were, place the suspect on the scene where he could have committed the crime but it does not prove that he did so. Furthermore, several other prominent suspects were also present at the same time. Laboratory investigations of the chemical composition of tobacco smoke and of the effect of smoke and smoke distillates on experimental animals have not so far yielded very much definitive information of a convincing nature concerning the causes of lung cancer in the human population. However, I think it is fair to say that laboratory evidence now available does lend some measure of support to the theory that smoking may be a factor in the development of lung cancer.

The only direct evidence on the matter has come from a number of independent investigations on human subjects, which have been described to you by Dr. Wynder. If these studies are reliable, the evidence from them, taken together with the circumstantial and indirect evidence previously mentioned, certainly builds up a strong case for an affirmative answer to the first simple question. In other words, almost all the evidence presented up to the present time does seem to indicate that cigarette smoking increases to some degree the probability that an individual will develop lung cancer.

Assuming for the moment that the first question is settled, let us now turn to the second question: How great is the effect of cigarette smoking on the probability of developing lung cancer? The aforementioned studies, while in complete agreement as to the first simple question, are by no means in agreement on this second and more difficult question. Wynder has given some figures on the percentages of smokers and nonsmokers found in patients with lung cancer compared with groups without lung cancer. What we really want to know (that is, from the practical side) is the probability that an individual who smokes will get lung cancer as compared with the probability that an individual who does not smoke will get lung cancer. An estimate may be made by applying a little simple arithmetic to the data as originally collected. After making the conversion we find that these studies do not agree anywhere nearly so closely as it first appeared.

Judging from the most extreme results in one direction, one might well conclude: (1) that cigarette smoking is the only really important factor in the causation of lung cancer; and (2) that owing to trends in smoking habits during the last few decades, death rates from lung cancer are certain to skyrocket to almost unbelievable heights within the next several years. However, the results of other similar investigations, while showing an association, do not seem to indicate that cigarette smoking is so all-important in the causation of this disease.

The discrepancy in results between these more or less parallel studies is really not very surprising for two reasons: (1) the details of procedure varied including the specific questions asked about smoking habits; and (2) more important, the experimental design used is not efficient from the standpoint of yielding reliable quantitative results that can be generalized to the population as a whole. In my opinion, the degree of influence of cigarette smoking as the causation of lung cancer is still an open question.

I should now like to mention briefly one more subject before turning to the

practical aspect of the problem. Broadly speaking, there are two major methods by which epidemiological studies can be conducted. These are usually called the "historical method" and the "follow-up method" or, as E. B. Wilson has so aptly phrased it, the "backward method" and the "forward method."

The "backward method" consists of questioning a selected group of patients with a specified disease about things that they have done or things that happened to them in the past. A so-called "control group" is similarly questioned, an attempt being made to select for this group individuals who appear similar to the patients in all respects except that they do not have the disease in question. A comparison is then made between the answers given by the two groups. The one virtue of this method is that under favorable circumstances it can be carried out quickly and at little expense. The disadvantages of the method are manifold, so much so that some statisticians believe that it leads to erroneous conclusions more often than to correct ones. Among the more important difficulties are: (1) psychological biases in answering questions dependent upon past experience, present circumstances, and the attitude of the interviewer or the phraseology of the questionnaire, (2) difficulties in selecting truly comparable experimental and control groups for questioning and the likelihood of unavoidable biases in this selection, and (3) a purely mathematical fallacy recently discovered by Joseph Berkson of the Mayo Clinic. The mathematical difficulty does not necessarily lead to erroneous conclusions, but it is very difficult to ascertain whether or not it does so in any particular instance.

The "forward" or follow-up method of study consists of obtaining information (by interview, questionnaire, or otherwise) about the habits or environment of a large number of people, none of whom is sick at the time these data are collected. The subjects are followed for a number of years and records are kept of all those who contract or die of a certain specified disease. The end results are then correlated with the facts gathered at the start

of the study. It is generally agreed that from the scientific standpoint this is the method of choice. It altogether avoids most of the major difficulties of the alternative method and minimizes the effect of the remaining difficulties. Furthermore, it yields answers directly in the form most suitable for practical interpretation and application. However, the method has several serious disadvantages: for example, (1) it is unavoidably time-consuming and may take as long as twenty years in some instances, (2) it is usually extremely expensive because of the large number of people who must be studied, and (3) it is extremely difficult to trace individuals for a number of years, particularly in America where people have a habit of moving around.

All of the studies of smoking in relation to human lung cancer previously described by Wynder were based on the backward method of approach, although the exact details vary. Because of the known difficulties with this method, certain investigators, including myself, are not completely convinced as to the validity of the results, in spite of the fact that a number of independent studies conducted in more or less the same way led to more or less the same apparent conclusions. In particular, I am not so concerned with the question of whether or not a cause and effect relationship exists between cigarette smoking and lung cancer as I am with the question of the degree of this relationship.

Now I should like to turn to some practical aspects of the problem. For the sake of the discussion, and because present evidence points in that direction, let us assume that cigarette smoking does to some degree increase the danger of contracting lung cancer. What can be done about it? Clearly, if the matter were as simple and as inconsequential as turning off the tap in the kitchen sink, we should eliminate cigarette smoking and have done with the danger no matter how small it may be. Obviously, it is not this simple as a few illustrations should serve to show.

I think you will agree with me that the American public has demonstrated a strong aversion to prohibition, so passing

a law is not a likely solution. Persuasion through education (once the facts are known) is certainly more palatable and more likely to succeed. However, it is by no means easy for heavy smokers to give up the habit or even to cut their consumption down to a moderate level. Furthermore, it is amazing to see how little effect danger sometimes has as a deterrent to people doing what they want to do. The 39,000 preventable deaths and untold injuries last year from automobile accidents is sufficient to attest to this fact.

Aside from this we must remember that we are not dealing with a scientific abstraction but with a real problem affecting most if not all of our population; and, in the everyday world, political and economic considerations cannot be ignored completely. Our allies in NATO are having a desperately hard time meeting the costs of defense and are constantly calling on us for more assistance. Great Britain, our strongest ally, is currently spending about £1,129,000,000 a year on defense and is currently collecting about 53 per cent of this amount (or £613,500,000 from taxes on tobacco. Denmark's defense budget is about 521 million Kroner as compared with 575 million Kroner collected from tobacco taxes.

Coming closer to home, our Federal Government spends a total of about 1.5 billion dollars a year to cover all activities designed to protect the health of our people—including the budget of the Public Health Service, medical services of the Veterans Administration, medical research, and aid to states. The annual federal revenue from tobacco taxes exceeds this amount by 100 million dollars. Even closer to home, New York State got 62 million tax dollars from tobacco last year.

If by any chance smoking should cease to be a popular habit, governments would have to find new sources of revenue—and that would not be easy or very pleasant.

I have brought up these facts not to create discouragement, but to show the magnitude of the problem with which we are faced. Clearly our government has an enormous financial stake in tobacco

sales. It also has a stake in the welfare of our people and in this instance the stake is more than 20,000 deaths from lung cancer a year with an ever mounting toll.

Again, what should we do and what are we doing about it?

In my opinion, the first step should be to find the facts of the matter in quantitative terms and beyond a reasonable doubt. Two years ago, the American Cancer Society started a study, using the follow-up or forward method, that we hope will yield conclusive answers. Volunteer researchers of the Society obtained information on the past and present smoking habits of 204,000 white men between the ages of 50 and 69. All of these men are being traced annually and when a death occurs the cause of death is ascertained from the death certificate. If the word "cancer" appears on the death certificate, then a study is made of the medical records to obtain the most reliable information available as to the primary site of the disease. Eventually, the data will be analyzed by cause of death and by type, amount, and duration of smoking as well as by other pertinent factors. However, even with such a large population under study, it will be at least another year and a half if not longer before enough data are collected to determine the facts on smoking in relation to lung cancer. As I said, follow-up studies, although most reliable, are necessarily time-consuming.

The first follow-up was started last November and our volunteers accomplished the remarkable feat of tracing more than 99.0 per cent of the men originally questioned. The second follow-up was started just two days ago, on November 1st. Of course, at this point I have no idea what the results of the study will be, but I should like to speculate briefly on two opposite extreme possibilities. The truth may and quite probably does lie somewhere between the two.

First, it may turn out that smoking has so little influence on the development of lung cancer that only a few very timid souls would take the danger seriously. In this event we would have to intensify our search in other fields to find the cause of

the tremendous rise in lung-cancer deaths.

Secondly, it may turn out that cigarette smoking not only greatly increases the probability of developing lung cancer but also markedly increases the death rate from other causes. Actually, there is some reason to believe that this may be so. In this event, I will hazard a guess that an appreciable number of people will give up smoking and the trend may well be cumulative. Smoking is largely a social habit that grew like a snowball once a small percentage of people were converted and it became socially the thing to do. Perhaps it might melt away in the same fashion once a moderate number of strong converts are made in the opposite direction.

But it will be months or years before the facts can be ascertained from the follow-up study. What should be done in the meantime?

Although it may turn out that smoking is relatively harmless, yet, considering their enormous financial stake in the matter, to say nothing of their moral obligation, it would seem sheer stupidity if both the Government and the tobacco companies do not immediately give strong financial backing to research into possible harmful ingredients in cigarettes and ways of removing them if such are found. In all justice, at least a tiny fraction of the gigantic tax on tobacco might be devoted to this purpose.

I will close with one other suggestion. Unless and until it is proved that smoking is the only culprit, we must not neglect research on the other possible causative agents.

Reference

Berkson, J.: Limitations of the application of four-fold table analysis to hospital data. *Biometrics Bull.* 2: 47-53, 1946.



EFFECTIVELY TO COMBAT CANCER OF THE LUNG:

The Patient's Responsibility

To have a chest film taken semi-annually, especially after 50 years of age.

The Surgeon's Responsibility

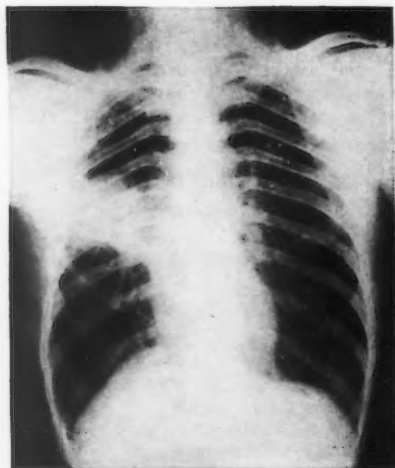
Immediate decision as to exploration; a total biopsy; radical removal of the malignant tumor.

The Family Doctor's and the

Roentgenologist's Responsibility

To be aware of the alarming increase in lung cancer and the consequent necessity for prompt diagnosis in "abnormal chest shadows."

Silent Lung Cancers Found



Man, aged 61. This shows a chance finding in a survey roentgenogram that was made in May, 1951. Later the diagnosis was proved to be epidermoid carcinoma of the lung.



Man, aged 43. A routine chest roentgenogram was made at the Dept. of Health in January, 1948. A shadow was seen in the right lung. Bronchogenic carcinoma was proved at autopsy.

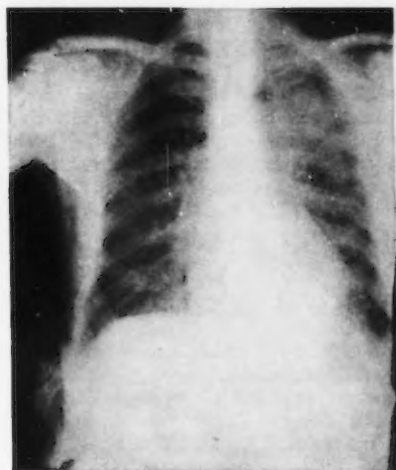


Woman, age unknown. Four and a half years ago she walked into a chest x-ray mobile unit because a friend was having a chest roentgenogram. The terminal bronchiolar carcinoma was later removed and the patient is living and well today.

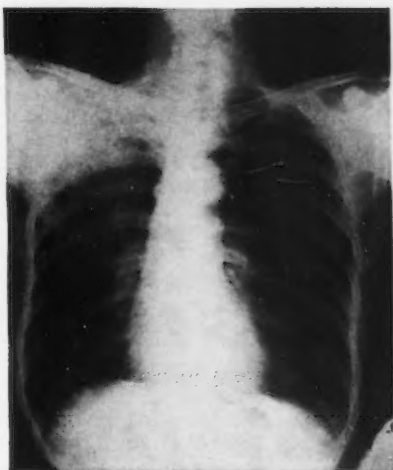


Woman, aged 43. A chest roentgenogram was made, routinely, by the Board of Education in January, 1949. It revealed a "coin" lesion in the upper lobe of the left lung. This was later diagnosed as bronchogenic carcinoma.

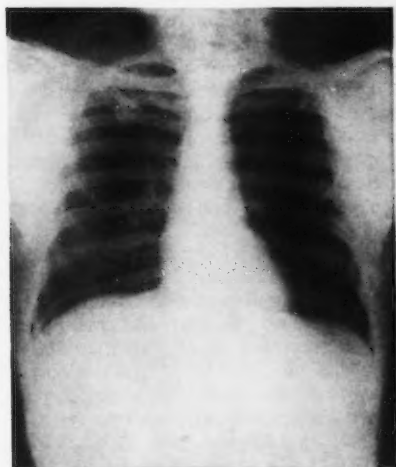
nd by Routine Chest X-ray



Man, aged 59. Roentgenograms were taken yearly at the place of employment until June, 1951, when a shadow was noted in the left upper lobe. This was later established as cancer of the lung.



Man, aged 55. Yearly routine visits were made to his local physician, who noted an opacity in the right upper lobe in the roentgenogram. The final diagnosis was carcinoma of the lung.



Man, aged 46. In 1948, a routine chest roentgenogram was made for civil service. The coin lesion in the right upper lobe proved to be epidermoid carcinoma. The local doctor delayed ten months before sending the patient for treatment.



Man, aged 54. The patient went to his local physician for a routine check-up and a routine roentgenogram disclosed a "mass" in the lower lobe of the left lung. Later a diagnosis of bronchogenic carcinoma was made.

Dividends and Defects of the Mass-Survey Method in Detecting Lung Cancer

Lewis W. Guiss, M.D.

The largest mass chest x-ray survey in history was completed in Los Angeles County during the last nine months of 1950. In this period a total of 1,867,201 persons had minifilms taken of their lungs. This particular survey was planned and executed to discover tuberculosis only. It was not until it was well under way that it became apparent that a large amount of cardiac pathology and possible lung cancer was being seen that required some attention.

It should be emphasized that the entire survey was organized as a tuberculosis case-finding mechanism and that the lung-cancer aspects of the project were regarded at that time to be entirely incidental. In the light of accumulating information, it now appears that lung cancer is rapidly becoming a problem of greater importance than tuberculosis. It may very well be that future chest x-ray surveys will be redesigned as primarily a screening procedure for discovering early lung cancer and that tuberculosis case finding will be regarded as of secondary importance. Such programs—unheard of in 1950—seem today to be the only method whereby early, asymptomatic, curable lung cancer can be discovered.

All persons whose 70-mm. films showed abnormal shadows suggesting significant chest disease were asked to return for a confirmatory roentgenogram. In the case of neoplasm suspects, this was a conventional 14×17-in. film. Of the nearly two million surveyed, 64,745 persons were asked to return for confirmatory roentgenograms, of whom 54,648 complied. The findings on the confirmatory roentgenograms are shown in Table 1.

Each confirmatory roentgenogram was reviewed by a diagnostic team consisting originally of a radiologist, an internist, and a tuberculosis specialist. It was felt that,

while tuberculosis and cardiovascular conditions were being picked up accurately, some neoplasm suspects might have been overlooked. The addition to each reviewing team of a young, well-trained thoracic surgeon with a high index of suspicion raised the percentage of neoplasm suspects measurably.

The 3500 Tumor Suspects

Of the 5646 confirmatory roentgenograms designated as showing "other chest disease," exactly 3500 were placed in the Chest Tumor Registry as constituting "chest-tumor suspects." This gives an incidence rate for tumor suspects of 1.9 per 1000 examined in the survey. This rate is significantly higher than in other surveys (Table 2) and may be attributed either to a high index of suspicion or to an actual increased incidence in Los Angeles County. Since the unit cost of the survey was \$0.754 per person, it required an expense of \$396.00 on the part of the entire project to discover each chest-tumor suspect. All readings that included possible, probable, or definite tumor diagnoses were accepted for registry.

As the cases were registered, a report was sent to the family physician, if the patient had indicated one, and the roentgenogram was made available to him. The patient was notified that the confirmatory roentgenogram showed the need for further study and urged prompt consultation with his physician. From the onset, every effort was made to have each person return immediately to his own physician for further study and care. If the patient insisted he had no doctor, he was referred to the appropriate panel of the County

From the Department of Surgery, University of Southern California School of Medicine, Los Angeles, California.

TABLE 1
Findings on Confirmatory
Roentgenograms

Essentially negative	14,344
Evidence of old healed disease	9,216
Tuberculosis	18,785
Cardiovascular disease	6,657
"Other chest disease" (included neoplasm suspects)	5,646
TOTAL CONFIRMATORY ROENTGENOGRAMS	54,648

Medical Society. Only when the patient was unable to afford private care, did the Registry make arrangements for the patient to be seen at the nearest part-pay or free clinic.

Delay a Big Factor

There was pronounced delay on the part of both physicians and patients in establishing a definite diagnosis in most of these cases. Two years after the inception of the survey and one year after its completion, about one fourth of the tumor suspects were still in the process of investigation with pending diagnoses. This is, of course, a result of a combination of apathy and lack of understanding on the part of the physician of the problems inherent in successful management of lung

cancer and lethargy and ignorance on the part of the patient as to the risk of procrastination.

The present status of the investigation of the 3500 lung tumor suspects is shown in Table 3.

Most of the categories are self-explanatory. The group designated as "tumor, clinically benign, not treated" includes all cases with a definite roentgen-ray report of chest tumor that, because they were asymptomatic, were never operated upon and because of their clinical course appeared to be benign.

The relatively large number of lost cases is due to two factors: Many subjects were visitors from out of the State, in Los Angeles County on vacation, and disappeared from hotels, motels, and trailer courts without trace. The other factor contributing to lost cases is that very little identifying information was recorded on the original form, making late follow-up difficult or impossible. Los Angeles County has an unstable population and, in any similar project, it is recommended that more identifying data be recorded at the time the minifilm is taken.

The distribution of the confirmed neoplasms is given in Table 4.

Half the Cases Never Treated

Of the 222 bronchogenic cases, 111

TABLE 2
Incidence of Possible Tumors Detected on 14×17-in.
Chest Roentgenograms in Other Surveys

Location	No. examined	No. of possible tumors (14×17 in.)	Rates/1000 persons exam.
Savannah-Chatham Co., Ga.	67,961	43	0.6
Gaston & Wayne Cos., N. C.	84,599	58	0.7
Milwaukee, Wis.	176,469	37	0.2
Minneapolis, Minn.	301,513	404	1.3
Washington, D. C.	439,927	373	0.8
Seattle-King Co., Wash.	368,129	261	0.7
Tacoma, Wash.	72,703	32	0.4
Spokane, Wash.	106,526	67	0.6
Salt Lake Area, Utah	162,351	107	0.7
TOTAL	1,780,178	1,382	0.8

TABLE 3

Present Status of Registered Cases

Chest neoplasm ruled out	2061
Chest neoplasm confirmed	340
Lesion metastatic to lung	105
Goiter	462
Tumor, clin. benign, not treated	295
Refused treatment	65
Lost	172
TOTAL	3500

have been operated on to date, giving an operability rate of 50 per cent. Of these, eighty-four were resected, an over-all resection rate of 38 per cent; or based on the number operated on, of 76 per cent. These are high operability and resectability rates but they should be high for such a survey group that presumably contains a large number of early asymptomatic lesions. It is of interest that, of the 222 patients with proved bronchogenic carcinoma, only eight, or 3.6 per cent, were less than 40 years of age. It is commendable that seventy of the 111, or 63 per cent, had their surgery in less than three months from the time of the mini-film. On the other hand, seventeen waited more than six months and one did not have his surgery until more than two years after his first roentgenogram. In addition there were 111 with confirmed bronchogenic carcinoma who never came to surgery at all for various reasons and therefore never had a chance for cure. A review of these untreated cases shows that usually these patients waited so long before consulting their doctors that they were inoperable when first seen professionally. Of the seventy-four with curative resections, forty-three are now known to be dead and thirty-one, or 40 per cent, are alive for periods varying up to two and one-half years.

Dividends

There can be no question but that the chest x-ray-surgery method is a somewhat expensive but effective method of discovering chest neoplasm suspects. In

fact it is only by such routine x-ray surveys that lung cancer can be discovered while still asymptomatic and in the silent and curable stage.

Asymptomatic early lesions may be expected to be almost routinely resectable if submitted to surgery promptly. This should result in higher cure rates.

Defects

1. Past surveys have been designed for tuberculosis case finding. In the Los Angeles Survey, 66 per cent of all mini-films were of persons less than 45 years of age. Only one third of the roentgenograms were taken in the age groups expected to develop lung cancer. Also the majority of the roentgenograms taken were of females who currently may be expected to develop only about 10 per cent of all lung cancer. If a roentgen-ray screening were to be designed primarily to detect lung cancer, it should be restricted to males more than 40 or 45 years of age, and thereby six times or more cases of lung cancer would be discovered as on a similar survey designed for tuberculosis detection. Had this been done in the Los Angeles Survey, each chest-tumor suspect discovered would have cost only \$66 instead of \$396.

2. The major portion of the potential salvage for lung-cancer cases discovered in the survey was lost because of failure to complement early detection with early treatment. Less than one third of the confirmed cases had their surgery in three months or less from the time of the mini-film, 20 per cent waited from four months to more than two years to be explored, and

TABLE 4

Distribution of Confirmed Neoplasms

Malignant	
Bronchogenic carcinoma	222
Sarcoma and other	34
Total malignant	256
Benign	84
TOTAL CONFIRMED TUMORS	340

exactly half (111) were never explored and hence never had a chance for cure. Patient and physician alike were responsible for this delay. Future mass screenings for lung cancer should be preceded and accompanied by a powerful educational campaign directed both to doctors and the public so that the potential salvage of such an x-ray survey may be realized.

3. An important difference between the problems of tuberculosis and cancer should be noted. In tuberculosis a single case-finding survey of a population, theoretically at least, can be expected to have a definite and sustained effect on the extent of the problem if all patients with infectious and incipient tuberculosis are given proper treatment, thereby removing potential and actual sources of secondary infections. A similar survey of a population for pulmonary cancer has no lasting value of this kind, since in the course of a few months the problem has recurred to its original extent. In other words, any cancer case-finding method must be a repetitive procedure for the population considered to be at risk.

Survey Method Effective

During the years 1950 to 1952 inclusive, a total of 1903 persons died of bron-

chogenic carcinoma in Los Angeles County. These death lists have been checked against an alphabetized list of those who had minifilms taken in the survey to determine what fraction of those who are to develop bronchogenic carcinoma may be expected to have minifilms taken in a survey and how often a survey might have to be repeated to be effective.

In 1950, the year of the survey, only twenty-seven persons who had NEGATIVE minifilms died of bronchogenic carcinoma that same year. The following year, 1951, 133 persons died of bronchogenic carcinoma who had negative minifilms in 1950; and in 1952, again, 146 persons died of lung cancer who had had negative minifilms during the 1950 survey.

These figures, still incomplete, show that the survey in 1950 did pick up most of the cases of bronchogenic carcinoma among those who submitted to the survey. They also show that the problem had returned to its original extent in one year, since approximately equal numbers died of lung cancer in the next two years who had had negative minifilms in 1950. It would seem obvious that the screening would have to be repeated at least every year and probably twice a year to be effective in discovering EARLY lung-cancer cases.

Fatalism about Cancer of Lung

Sir—The great majority of smoking doctors seem to have adopted a fatalistic attitude towards their developing cancer of lung. They usually argue that if they are going to develop cancer of lung, carcinogenesis has doubtless been going on in their bronchial stems for years, so why should they bother to stop smoking now, when it would almost certainly be too late?

The carcinogen has not so far been found, but it is probable that carcinogenesis resulting from chronic irritation by tobacco smoke goes on all the time in the bronchial stems of all smokers, to an extent which corresponds mainly with the heaviness of their smoking. Only occasionally does carcinogenesis go on to carcinoma, and so long as no symptoms of cancer of lung have developed, there is a good chance that stopping smoking—cutting off fresh supplies of carcinogen—will prevent this happening. Doll and Hill (*Brit. Med. J.* 1952, ii, 1275) found that out of 1350 male smokers who developed cancer of lung, 70 (5.1%) had given up smoking for a year or more, whereas in the case of 1296 matched control smokers, the corresponding figure was 124 (9.6%).

Johnston, L.: *Letters to the Editor. Lancet* 1:244, Feb. 28, 1953.

Chest Roentgen-Ray Screening for Cancer of the Lung

G. Howard Cowen, M.D.

If we are to reduce the death rate from lung cancer, earlier diagnosis is a must. A satisfactory surgical technique has been developed and the operative mortality is low. This has little practical value if cases continue to be presented to the surgeon in the advanced stages.

Our only hope at the moment of bringing to light the "silent" or asymptomatic lung cancer is the mass chest x-ray survey. Experience to date would suggest that between seven and ten cases of primary lung cancer per 100,000 persons examined can be discovered in this manner. Unfortunately most cases will be non-resectable either at the time the first roentgenogram is taken or by the time final diagnosis is established. We have the tool but it remains for us to make it work.

A basic need is to get large numbers of persons more than 40 years of age, particularly men, to submit to chest roentgenograms at regular intervals. The present coverage is not sufficient to find enough cases to alter the death rate significantly. This is not going to be easy and will require an intensive promotional campaign jointly sponsored by the medical society, the cancer society, and the tuberculosis association. The degree to which such groups can co-ordinate their activities is well exemplified by the Boston Chest X-ray Survey conducted during 1949 and 1950 and the Los Angeles County Survey of 1950 and 1951. A central steering committee was appointed with special subcommittees for cancer, tuberculosis, and heart disease. The practicing physicians were appraised of the program well in advance and, as a result, the co-operation was excellent in regard to providing follow-up information.

In the past, the tendency has been to give worth-while instructions to the public and not provide the means of carrying

them out. It might be well to determine first if facilities and personnel are available to carry out such a plan. If not, they will have to be secured. The voluntary and official agencies concerned can do much in such a program. The most potent force, however, should be the practicing physician. He is the one who can get his patients to take advantage of the chest x-ray survey if he will take the time to do so. The passive attitude exhibited toward the tuberculosis case-finding program will have to be changed. The time has come when the physician must devote more time to health education of his patients in proportion to the time he spends curing them of their ills. The mere approval of the local medical society will not be enough. Each doctor will have to do his part.

The attitude of the public will have to be materially altered. As long as people continue to give silly excuses for not submitting to chest roentgenograms (anyone who doubts this should work for one day with a mobile chest x-ray unit trying to solicit the local residents) there is much to be done along educational lines. Many appear for roentgenograms because of the existence of symptoms for which they should have already sought medical care. Others, intentionally or otherwise, give erroneous information to the record clerk and consequently the discovery of suspicious findings can not be used to that person's benefit. Some are resistant to a diagnostic work-up in the presence of suspected lung pathology. Later these seek medical care because of well-developed symptoms—unfortunately too late. All this plays a part in patient delay.

There must be a high index of suspicion

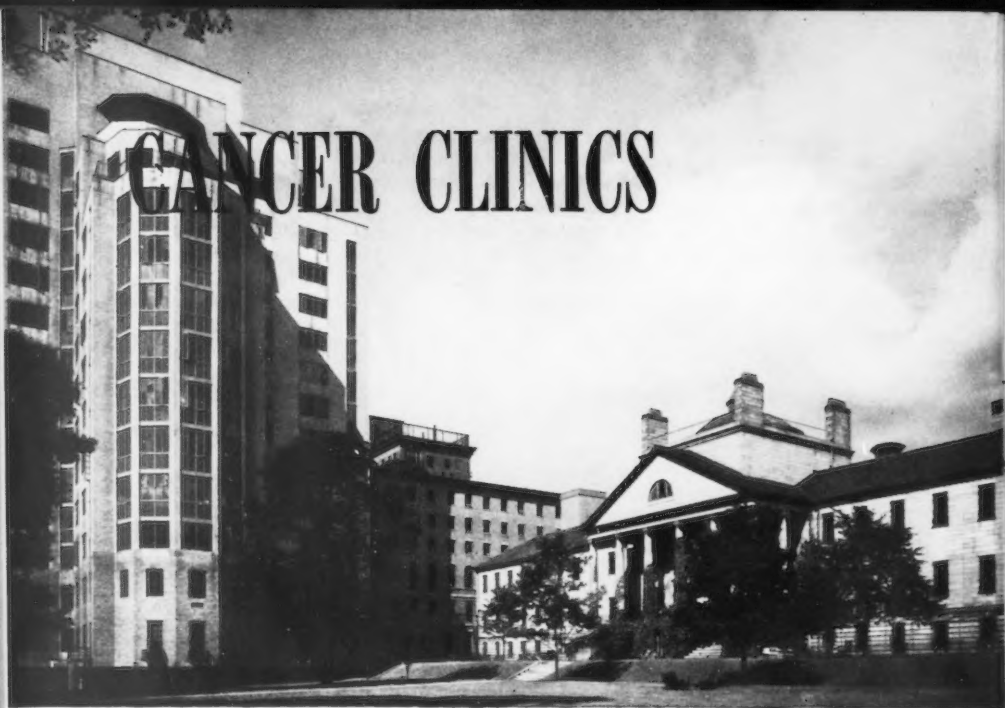
From the Division of Hospitals and Chronic Illness, Illinois State Department of Public Health, Springfield, Illinois.

on the part of the survey film reader. When, as a result of a chest x-ray survey on a community basis or as part of a hospital admissions program, a person with suspicious lung findings is brought to the attention of his doctor, he must immediately and systematically be given those examinations that will aid in establishing the final diagnosis. Consultation facilities should not be ignored. The time factor is most important.

The physician's first job will be to get the patient in for counseling. This may not be easy. A chest retake using 14×17-in. film is next in order and must not be delayed. Unfortunately it is not superfluous to say that the roentgenogram should be taken by a qualified person and on modern equipment. In a high percentage of cases this will establish the presence or absence of malignant tumor. Group conferences over roentgenograms hard to interpret are of great value. Further roentgenographic studies are made as indicated. It can not be emphasized too strongly that the radiologist is an important link in the diagnostic chain. Other diagnostic steps may include cytological examination of sputum or bronchial washings and bronchoscopy with direct biopsy. Finally, there will be a group that can not be diagnosed by any of these procedures. The answer in such cases can only be obtained by exploratory thoracotomy. This procedure has a very low operative risk. The same philosophy on the part of physician and patient must be developed toward exploratory thoracotomy as toward exploratory laparotomy. When all other diagnostic measures are unproductive, it has to be done! Many primary lung carcinomas do not receive early and effective treatment because prolonged attempts are made to establish the presence of the tubercle bacillus. In only about 1.5 per cent of cases of pulmonary tuberculosis is lung cancer also present. It

has been suggested that there are now enough adults who are tuberculin negative so that the use of the tuberculin test might prove helpful in some cases in eliminating the possibility that the lesion in question may be due to the tubercle bacillus. Delay in diagnosis on the part of the physician is usually not due to laxity, but rather to misinterpretation of the findings because the prevalence of lung cancer is not sufficiently appreciated. It is now the most common cause of death from cancer in men, particularly between the ages of 40 and 60 years.

As stated previously, to be effective, a program of chest roentgen-ray screening for lung cancer must be extensive. Fortunately the tuberculosis case-finding equipment and the methods are available and it only remains to put them to an additional use. There is one basic difference, however, between pulmonary tuberculosis case finding and the search for early cases of lung cancer. When a case of tuberculosis is discovered, removed from further contact with the public, and treated, the chain is broken and further cases from this source are prevented. Finding one case of lung cancer does not prevent another. Each case has to be searched for separately. The job will therefore be harder. Any such project will have to be set up on a long-term basis. There will have to be the same concerted effort as has been exhibited in teaching women self-examination of the breast for the early detection of cancer. The sporadic measures now being employed do not offer much either in result or information. Lung cancer is high on the priority list of all cancer and deserves an equitable amount of attention. Since the use of chest roentgen-ray screening is the *modus operandi* of choice in detecting early cancer of the lung, it behooves us to try to make it work with a well-planned and intensive program.



Weekly Clinicopathological Exercise

A 50-year-old woman entered the hospital for evaluation of an abnormal shadow discovered in a routine roentgenogram of the chest one week previously.

For about sixteen years before admission the patient had complained of post-nasal discharge and productive morning cough and had treated herself with oily nose drops. She had frequent upper-respiratory infections and several times each winter would take to her bed with cough and fever diagnosed as "chronic bronchitis." Nine years, five years, and five months before admission she was hospitalized because of attacks of right-sided "lobar pneumonia," which responded to chemotherapy and antibiotics. About six months before admission she had an attack of "virus pneumonia."

Fifteen months before admission she had a small hemoptysis of bright-red blood that welled up suddenly from her throat after some difficulty in swallowing a cough drop. There was no associated pain, fever, or malaise of any description. A

chest roentgenogram taken by her physician was said to have shown a "cloudy condition." Two forty-eight-hour sputum cultures were negative for acid-fast bacilli. The patient began to keep a daily temperature chart, which remained within normal limits at all times. A month after the hemoptysis the patient was studied at this hospital as a medical out-patient. Physical examination was unremarkable. The blood and urine were within normal limits, but the sedimentation rate was 41 mm. per hour. The roentgenograms taken in another hospital were reviewed, and the findings were believed to be consistent with old healed pulmonary tuberculosis. Bronchoscopic examination was considered but was deferred because the bleeding had stopped.

Periodically roentgenograms were taken at a tuberculosis sanatorium and the re-

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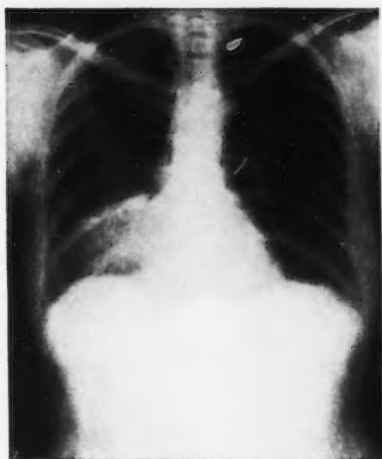


FIGURE 1

ports sent to her physician. In addition, she made periodic visits to the Pulmonary Clinic. No essential changes were noted in the roentgen-ray findings until six weeks prior to admission, at which time a large shadow at the right base was noted. Roentgenograms taken here two weeks later showed a rounded mass, 7 cm. in diameter, projecting from the wall of the anteromedial right base. This was independent of both the heart and the diaphragm. The upper right-lung field showed mottled density, especially at the periphery. The diaphragm was normal in shape and contour. The left-lung field, heart shadow, and great vessels were unremarkable (Figs. 1, 2).

The family history revealed that the patient's mother, who died at the age of 80 of arteriosclerosis and hypertension, had had repeated small hemoptyses throughout her life. Two half-sisters died of pulmonary tuberculosis forty-one and forty-three years before the patient's admission.

On physical examination an area of dullness was found over the right anterior chest, associated with decreased whispered voice and breath sounds and tenderness to direct palpation. The lungs were otherwise clear and the heart normal. The mar-

gin of the liver and tip of the spleen were just palpable below the costal margin. Grade I-to-II hypertensive retinopathy was present. There were large varicosities on both lower extremities.

The temperature was 99°F., the pulse 80 and regular, and the respirations 20. The blood pressure was 180 mm. of mercury systolic, 110 diastolic.

Urinalysis was negative. Examination of the blood revealed a hemoglobin of 13.0 gm. and a white-cell count of 5600, with 66 per cent neutrophils, 24 per cent lymphocytes, 8 per cent monocytes, 1 per cent basophils, and 1 per cent eosinophils. The sedimentation rate was 50 mm. in one hour. A cytological examination of the sputum was negative for malignant cells.

Chest roentgenograms showed the mass in the right thorax to have definitely enlarged. Fluoroscopically it appeared to move synchronously with the lower anterior chest wall. Barium-enema and barium-swallow examinations were negative. There was no evidence of herniation through the right leaf of the diaphragm. The kidneys appeared to be normal. The spleen was larger than normal, and the liver was noted to be low in position.



FIGURE 2

After an uneventful period of observation, an operation was performed on the seventh hospital day.

Differential Diagnosis

DR. EDWARD D. CHURCHILL: A 50-year-old woman was admitted to the hospital, as so many people are these days, for an evaluation of an abnormal shadow discovered in a chest roentgenogram.

For about sixteen years she had had vague respiratory symptoms. That is rather typical of what repeated questions finally elicit from a patient and is probably irrelevant. I do not think the oily nose drops had anything to do with this patient's condition. Like almost everyone, she had frequent upper-respiratory infections, but unlike most others she took to her bed several times each winter with chronic bronchitis. The patient also disclosed the fact that fifteen months before admission she had what a physician called hemoptysis. The chest roentgenogram taken by her physician was reported as cloudy. This means nothing; perhaps she breathed when the film was taken.

The patient began to keep a daily temperature chart, indicating that she was becoming disturbed about her condition, but whether this was because she thought the physicians believed she had something or because she felt ill is hard to say. At any rate the temperature-taking yielded no information. A month after the hemoptysis and fourteen months before admission, she came to the Out Patient Department. Examination was negative except for a sedimentation rate of 41 mm. per hour. I have not the slightest idea what that means. The roentgen-ray findings were consistent with an old healed pulmonary tuberculosis. Bronchoscopy was considered, I presume because of the hemoptysis, but was deferred. Bronchoscopy is a very important procedure when a patient spits up blood.

Roentgenograms were made periodically at a local tuberculosis sanatorium and the reports were sent to her physician. In addition she made regular visits here to see Dr. Pittman in the Pulmonary

Clinic. Nothing was found in the chest until six weeks prior to admission. That is not quite correct, however, as she did show a shadow prior to that time.

After admission to the hospital the physicians dug out the fact that the patient's mother lived to a ripe old age and had had small hemoptyses all her life. There were also two half-sisters who died of pulmonary tuberculosis. I do not know through which side of the family they were related, but because the mother lived to a ripe old age I can assume that perhaps they were her mother's daughters, so that there was familial distribution of tuberculosis. Nothing abnormal was found on physical examination.

The patient was said to be in no distress. You cannot make me believe that. I think she had the "daylights scared out of her." I do not think she had any pain, but one cannot take his own temperature, have hemoptysis, and run to physicians as this woman did without being in some mental distress.

All this reduces the problems to a guessing game on roentgen-ray shadows, and I am delighted to have the radiologist hold forth.

DR. JOSEPH HANELIN: We have chest roentgenograms, made elsewhere, dating back eight years. In those taken eight years before admission, there is nothing of note other than calcific and fibrotic scars in the right lung of rather minimal extent. The heart and diaphragm appear normal. On carefully perusing the old roentgenograms, I think the first evidence of disturbance in this patient's chest is shown on those taken a year before admission, at which time there is just visible at the right base, along the heart margin and through the heart shadows, a mottled density that had not been present previously.

DR. CHURCHILL: How about the apex?

DR. HANELIN: I do not think the lesion there had progressed to the apex. In films taken four months and seven months later there is evidence of enlargement of the density at the right base. No lateral views were taken at that time. In the films taken a week before admission, when the lesion was first discovered, it is of large size. In

the films made on admission, the mass lies anteriorly on the right and appears, particularly in the oblique view, to be distinctly separate from the diaphragm (Figs. 1, 2). On fluoroscopy it moved synchronously with the anterior chest wall, and in all the films in which the mass attained any size it seems to be consistently confined to the level of the third, fourth, and fifth ribs anteriorly. Also noted in the examination a week before entry is the first appearance of transverse linear streaks in the right upper lung. There is also some suggestion of an enlarged lymph node at the right hilum. As to the statement of no evidence of herniation, a shadow at this level should always be regarded as a possible omental hernia until proved otherwise. Barium-enema and barium-swallow examinations were made. In the presence of omental hernia the transverse colon and stomach will usually be pulled toward the hernia. This was not true in this case. In the last set of films, made three weeks after the first Massachusetts General Hospital examination, further enlargement of the mass at the right base has occurred.

DR. CHURCHILL: The signs of omental hernia through a parasternal aperture, the foramen of Morgagni, are always looked for in relation to a lesion but are present only when the omentum has been drawn up into the chest. This would not exclude a diagnosis of intrathoracic protrusion of peritoneal fat.

DR. HANELIN: No; not at all.

DR. CHURCHILL: I dislike discussing this case, because I see so much harm done these days from using clinicopathological-conference techniques on living patients before the course to be pursued is definitely charted. I would like to say for the record that I know I do not know what this shadow represents. There should be no pretense. Why is that important? Because too much emphasis is placed on making guesses about what the shadow may represent, instead of arriving at a clear-cut decision as to what course of action is advisable. The patient cannot understand why, after roentgenograms have been made, the physician does not

seem to know what is there. The physician gets his mind centered on the precise identification of a shadow rather than on what should be done with a particular patient under these circumstances. As a result, patients that I see in consultation are likely to be in an antagonistic, thoroughly bewildered and confused state of mind.

It is very simple to explain to the patient something about the type of evidence that the roentgenograms provide. Very often I use the remark "You know, the x-ray examination does not tell us precisely what is wrong." This comes as a surprise, because by this time the patient has been forced to the conclusion that the roentgenogram is precise but the doctors are hazy. "Do you remember," one may continue, "when somebody put his hands in front of a light and cast a shadow on the wall and made you think it was a horse? That's what we are dealing with—a shadow picture." Then the patient begins to understand why his physicians seem a bit confused. In the meantime the consultant is making up his mind about what he will recommend under the circumstances. He should not hold a clinicopathological conference in front of the patient but should say: "I don't know what this is, but I do know what to do about it."

There is no question whatsoever about what should have been done about the patient under discussion. I must confess to an almost complete lack of interest in guessing what produced the shadow. There is no train of logical reasoning or experience that might enable anyone to make a preoperative diagnosis in this case. With a lump that is accessible to palpation, certain physical signs may help determine its nature—hardness, firmness, mobility, and so forth. One cannot palpate a shadow. If lumps in the chest could have been felt, chest surgery would have developed more rapidly.

Having warned against guessing games in front of the patient, we can proceed to the conventional practice of these conferences. The position and size of the mass are important. We know that she had had a primary tuberculous infection; a Ghon

tubercle lies behind the shadow. Possibly she, along with her half-sisters, received a dose of tubercle bacilli from the blood-spitting mother. Is the shadow an old or a fresh tuberculous infiltration? It is hard for me to interpret it as tuberculosis. Occasionally a small localized pleural effusion will occur in tuberculosis, but that is not likely in this case, particularly in the presence of an established primary infection dating back many years. I do not believe that the present condition was connected with the tuberculosis but that the patient had inactive tuberculosis in addition.

I have already said that the mass could represent a hernia in the diaphragm, despite the studies that suggest otherwise. If it was found to be a hernia through the foramen of Morgagni, it would have contained properitoneal or propleural fat, not omentum or bowel. Could it have been a simple fatty tumor? Yes; it may have been a lipoma. Against that is the evidence of increase in size. I do not think it is logical to consider it a thoracic lipoma, because it was expanding too rapidly.

Was it malignant tumor? I think not. The position is against it; it was not in the lung by roentgen-ray examination, was it?

DR. HANELIN: There were two schools of thought. It certainly was in the thoracic cavity, but whether it was in the pleural space or in the lung parenchyma was seriously debated.

DR. CHURCHILL: I do not believe a shadow in such a position was in the lung. One might be fooled, however. It may have been a tumor close to the lung, but it does not appear to be based on the lung. If it was not based on the diaphragm or on the lung, where was it based? That brings up two other diagnoses. Its position is a favorite one for a pleuropericardial cyst. Such cysts may be completely cut off from the pericardium and contain what we loosely call spring water—it actually looks like spring water. Such cysts do not grow as rapidly or expand as this shadow had done. Moreover, it is large for the usual pleuropericardial cyst that occupies this angle. However, as you look at the roentgenograms the only point at which

the shadow is attached, and the oblique film shows it very nicely, is on the lateral surface of the pericardium, so anatomically it could be a diverticulum of the pericardium, rather than a pleuropericardial cyst that had been embryologically pinched off from the pericardium.

For the record I shall make the diagnosis of pleuropericardial cyst.

DR. TRACY B. MALLORY: I am in hearty agreement with much that Dr. Churchill has said about the comparative unimportance of a correct preoperative diagnosis in comparison with the great importance of a decision concerning what to do about the lesion. In the course of about a score of years since Dr. Cabot's retirement the emphasis in clinicopathological conferences has shifted from primary interest in diagnosis to explanation of how the demonstrated pathological lesion or lesions explain the patient's clinical course and symptoms. The latter may sometimes be a difficult task for the pathologist because the evidence is not always adequate.

DR. HELEN S. PITTMAN: This patient was referred to us somewhat over a year before admission because she had spit blood. She actually had spit less than a teaspoonful of blood, and she had stopped bleeding when we saw her. We thought she had bled from around a little bit of calcium in an old tuberculosis lesion, and we were not very much worried. If she spit more blood, she was to come back at once; otherwise she was to come back in a few months for a check-up. When she came back for the check-up we found that she had spit no blood and was all right. She came back six months later when the roentgenograms showed this large mass and it was decided to send her into the hospital. On physical examination there was one thing that impressed me: that is, that she spit a small amount of sputum into the cup each day and there was a small bit of blood in the one specimen I saw. She had marked rib tenderness over the shadow. Dr. Kane is the one who really "carried the ball."

DR. LEWIS W. KANE: I have nothing to add except that she was very apprehensive because of the family history of tubercu-

losis. When she had a hemoptysis the size of a dime, she was sure she had tuberculosis. The shadow along the right margin of the heart was mentioned, I believe, when the serial roentgenograms were taken. But she had had a bout of pneumonia on that side just before that, and there was some question whether this was not a residual condition. Unfortunately, I did not see her until one year later. By that time the shadow had increased so markedly in size that she was sent to the hospital for thoracotomy.

DR. EDWARD B. BENEDICT: I would not defer bronchoscopy just because bleeding had stopped. I should like to bronchoscope a patient of this sort with a mass and with hemoptysis on the basis that she very likely had a carcinoma.

DR. PITTMAN: The bleeding occurred a year before any shadow was identified in the chest, and there was only one episode of a small amount of bleeding, which we thought was from the calcium. All we could see was calcium.

DR. BERNARD JACOBSON: Are you not slightly worried by the spleen's getting bigger?

DR. CHURCHILL: I have no evidence that it was enlarged.

DR. HANELIN: We were not at all sure that the spleen had changed in size. Eight years before admission the spleen also looked somewhat oversized.

DR. LAMAR SOUTTER: We believed there was some urgency in operating on this woman, because we thought the shadow in the lung was probably a malignant tumor.

Clinical Diagnosis. Malignant tumor of lung.

Dr. Churchill's Diagnosis. Pleuropulmonary cyst.

Anatomical Diagnosis. Malignant lymphoma, reticulum-cell-sarcoma type, of lung.

Pathological Discussion

DR. SOUTTER: When the chest was opened the lung was densely adherent to

the chest wall, with thick edematous adhesions. As we severed these we found a tumor lying in the middle lobe. It had invaded both the upper and lower lobes and the anterior chest wall. We biopsied the tumor. The pathologist confirmed the fact that it was a malignant neoplasm. We believed a resection would not benefit the patient, as there was not only local invasion but distant metastases to the peristernal lymph nodes. Therefore nothing further was done.

DR. MALLORY: A biopsy specimen was taken that showed a frankly malignant tumor that at one point was invading striated muscle. I assume from Dr. Soutter's description that it was an intercostal muscle rather than the diaphragm.

DR. SOUTTER: That is correct.

DR. CHURCHILL: The earliest roentgenogram that showed a shadow was taken how long before admission?

DR. BENEDICT: About sixteen months.

DR. CHURCHILL: That could have been the beginning.

DR. BENEDICT: That was about the time she had the hemoptysis.

DR. CHURCHILL: Was there ever hemoptysis that would have permitted localization by the bronchoscope?

DR. BENEDICT: I do not know.

DR. HANELIN: I think one would have to look very closely and be very suspicious to see an abnormal shadow in that roentgenogram. Other views and grid films would have been helpful. Six months later there was a very definite shadow that was interpreted as pneumonia.

DR. BENEDICT: Bronchial washings might have shown more than the sputum. I cannot quite agree with your philosophy, Dr. Churchill. When one raises the question of cancer in a patient's mind, the sooner he operates the sooner he has put the patient's mind at rest.

DR. CHURCHILL: You misunderstood my point. I agree with you completely. However, when the question of an abnormal shadow comes up and no further evidence can be obtained, one should concern himself with what should be done rather than with a precise definition of what it is.

DR. BENEDICT: The question of tumor had been raised.

DR. CHURCHILL: If one argues about the identity of the shadow, he loses his opportunity to do the right thing.

DR. PITTMAN: Here we missed our opportunity to identify anything in the roentgenogram.

DR. CHURCHILL: There was not much to see.

DR. PITTMAN: It can be seen there now, but it was not noted until a year after the roentgenograms were taken.

DR. MALLORY: The histological examination showed without any question that the tumor belonged in the lymphomatous group. There was some difference of opinion among members of the staff concerning which subtype of the lymphomatous tumors it should be placed in. I personally thought it should be called a reticulum-cell sarcoma, although the possibility of the sarcomatous form of Hodgkin's disease could not be absolutely eliminated. Some authorities like Dr. Philip Custer doubt that there is a true distinction between these two forms.

DR. HANELIN: Was any lymphatic spread evident in the right upper lung?

DR. SOUTTER: No, I do not think so. The right upper lobe of the lung was somewhat compressed by the tumor, but, except where it had been locally invaded, there was no tumor within it or in the interlobar nodes.

DR. MALLORY: It would be impossible, from the small specimen we received, to decide whether or not this tumor involved the lung tissue. We shall have to take the surgeon's gross exploration for settlement of that issue.

DR. SOUTTER: I gave you two specimens, one from the chest wall and one from the lung.

DR. MALLORY: There was no recognizable lung tissue, grossly or microscopically.

DR. CHURCHILL: I do not know whether anyone present heard Tallulah Bankhead's version of "Casey at the Bat." Casey went home after having struck out. His wife asked him what happened. All he could say was: "I don't know; I just don't know."

Color Television

Date	Program Subject	Participants
April 7	Treatment of Recurrent Cancer of the Cervix	Alexander Brunschwig and Attending Staff, Memorial Center.
April 14	Cancer of the Genitourinary Tract	Willet F. Whitmore, Victor F. Marshall, and James L. Green.
April 21	Tumors of Bone	Bradley L. Coley, Norman L. Higinbotham, and Robert E. Carroll.
April 28	Moles and Melanomas	George T. Pack.
May 5	Lymphoma and Leukemia	Lloyd F. Craver, Henry D. Diamond, Joseph H. Burchenal, David A. Karnofsky, Henry J. Koch, and Sophie Spitz.
May 12	Tumors of Childhood	Harold W. Dargeon and Attending Staff, Memorial Center.
May 19	Hormonal and Chemical Treatment of Cancer	Rulon W. Rawson, Joseph H. Burchenal, David A. Karnofsky, Olaf H. Pearson, and Joseph E. Rall.
May 26	Treatment of Patients with Advanced Cancer—Analgesia and Psychiatry	Raymond W. Houde, Arthur M. Sutherland, Charles E. Orbach, Morton Bard, and Ruth B. Dyk.
June 2	Frontiers of Research	Cornelius P. Rhoads.



DOORS DILEMMAS

Q *I have a 53-year-old nullipara who is three years postmenopause. One year ago, at the time of an "annual checkup," a small (2×2 cm.) fibroid-like tumor could be felt on the anterior surface of the uterus. She was asymptomatic at that time. In the last month, however, she has had two episodes of slight-to-moderate vaginal bleeding. The cervix is clean and the mass is unchanged in size and consistency. Because of a mild, diet-controlled diabetes, surgery has been deferred for what is an apparent benign fibroid. As long as the bleeding can be controlled, is there cause for concern about the possibility of malignant change in the tumor?*

A This patient should be treated just as though no "fibroid" was suspected or mass palpated. While it is true that subserous fibroids are frequently associated with the intramural and submucous varieties that produce bleeding and that only rarely does a benign fibroid undergo sarcomatous change, the important consideration here is that the presence of vaginal bleeding after the menopause is one of the commonest symptoms of endometrial cancer. Without further delay this patient should have an endometrial biopsy by adequate curettage to rule out carcinoma of the endometrium.

Q *A 46-year-old man with polycythemia vera, well controlled by occasional administration of radioactive phosphorus, finds he must move to another city at a*

much higher altitude. Is this undesirable. His only complaint at present is of intermittent but distressing paresthesias.

A Patients with polycythemia vera, residing for long periods of time at very high altitudes, might possibly develop some erythrocytosis (owing to the altitude) superimposed on the recurring polycythemia. However, if the disease is controlled and the hemogram normal, reasonable change in altitude would be most unlikely to cause trouble. The paresthesias that frequently accompany this disease may be the result of dilatation of the blood vessels of the skin and sometimes persist even when there is a normal blood-cell count. Sudden changes in temperature often intensify the paresthesias and these patients should be instructed to avoid or modify those temperatures that cause discomfort.

Q *I am anxious to avoid surgery for a 71-year-old man who has moderately severe heart disease and a right hemiplegia. However, he has recently complained of gastrointestinal trouble and roentgen-ray examination discloses multiple ulcerations in the stomach. The symptoms have been completely relieved after two weeks of a medical regimen. What further measures, besides exploratory laparotomy, should be undertaken to rule out the presence of gastric cancer?*

A Multiple gastric ulcerations are

usually benign. Since the patient's symptoms have responded so promptly, it is unlikely that his ulcerations are malignant. The medical therapy should be continued with repeated roentgen-ray studies at one, three, and six months' intervals. Only in the event of further evidence of ulceration is surgical exploration indicated.

Q *Is there general agreement that most so-called senile keratoses should be removed to prevent the development of squamous-cell carcinoma?*

A Since both basal- and squamous-cell carcinoma are known to develop in an appreciable number of persons with senile keratoses, it is wiser to treat the benign lesion than to await its possible transformation to a malignant one. Such keratoses, especially those occurring on exposed skin surfaces or surfaces subjected to constant irritation, may be removed surgically or treated with electrodesiccation, carbon dioxide, or radiation therapy.

Q *What is the prognosis in cancer of the larynx?*

A The presence or absence of cervical metastases and the size of the tumor are the two important factors in determining prognosis. A five-year-cure rate of 95 per cent may be obtained by partial laryngectomy or laryngofissure when the tumor on the vocal cord measures 1 cm. or less in diameter. The cure rate is substantially lower for larger lesions of the intrinsic larynx and for any lesion of the extrinsic larynx.

Q *A 28-year-old ex-G. I. complains of a small, painful ulcer of four weeks' duration that appears on the right, posterior lateral surface of the tongue. Blood serology is negative for evidence of lues. What diagnostic procedures should be followed?*

A Cancer of the tongue in young people occurs infrequently and is often not even suspected until the lesion is well advanced. Serological tests should, of course, be done to rule out luetic ulcer, but the importance of early and adequate biopsy cannot be overemphasized. If the diagnosis of cancer is established, the choice between radiation and surgery as treatment should be made by the physician who will assume responsibility for the patient. Whatever the choice of therapy, it should be thorough and adequate, since each unsuccessful attempt at treatment for residual or recurrent disease decreases the possibility of cure by half.

Q *What is the explanation for the sudden development of petechiae over the lower extremities and in the oral mucous membranes of a patient with advanced metastatic breast cancer who is receiving no medication other than testosterone? What is its significance?*

A In the absence of other etiological causes, the development of hemorrhagic tendencies in patients with carcinomatosis suggests extensive invasion of bone marrow by cancer cells, resulting in depression of platelet formation. It is a serious development with poor prognostic significance. Occasionally ACTH or cortisone, plus the frequent administration of blood, is temporarily helpful.



new developments in cancer

N, P, and K Storage . . .

When patients have progressively growing cancers, they store nitrogen, phosphorus, and potassium readily. When therapy is effective phosphorus is excreted in large quantities—much more so than nitrogen, which apparently is shifted from the shrinking or destroyed tumor back into the normal tissues of the host. These are some of the findings of Fenninger and others (University of Rochester) in studying tumor-host metabolic relationships. Cancer patients retain much more phosphorus and potassium than do normal people or those chronically ill with non-neoplastic disease. The latter store as much nitrogen as cancer patients do. The evidence indicates that when the diet is not adequate for the needs of both host and tumor, nitrogen is transferred from the host to the tumor.

Virus Susceptibility . . .

Another difference in the infectibility of embryonic and adult tissues has come to light in experiments by Greene (Yale University). Fragments of embryonic rat skin were exposed to the virus of Shope rat papilloma. Transplanted to the brains of adult animals, the tissues showed typical papilloma formation. Adult tissues so

exposed and implanted did not respond. And neither did adult or embryonic tissues of guinea pig, hamster, and mouse.

Role of the Thymus . . .

The thymus has been further indicted in the pathogenesis of some kinds of mouse lymphomas by Kaplan, Brown, and Paull (Stanford University). The investigators irradiated a strain of mice (C57Bl) that develop lymphoid tumors invariably within ten months of irradiation. However, when as late as twelve weeks after irradiation the scientists removed the animals' thymus glands, later tumor development was suppressed completely. As a matter of fact, two mice whose excised thymus glands showed tumors were cured. When homologous thymus glands were implanted in irradiated and thymectomized animals, the incidence of lymphoid tumors rose significantly.

Doctors Diagnosing Own Cancers . . .

Robbins and others (Memorial Center, New York) have shown in early studies that physicians share a large part of the responsibility for late diagnosis and treatment of cancer. Now the group has gathered statistical data to indicate that physicians are just a shade less alert than

laymen when it comes to detecting their own cancers. Moreover, they are not much better than laymen in finding physicians who diagnose and treat their cancers promptly and properly. The writers expressed disappointment in finding that physicians: (1) are not sufficiently concerned about the early diagnosis of such diseases in their own persons, (2) permit an unjustifiable delay before curative treatment is started, and (3) choose for their initial consultant a physician whose culpability for delay is approximately as great as that of general practitioners.

Lung Cancers Among Nonsmokers . . .

A recent report by Doll (British Medical Research Council) concludes that one in five of the lung-cancer deaths that occurred in persons aged 25 to 74 years in 1950 may be attributable to causes other than smoking. A nonsmoker is defined as a person who has never consistently smoked for as long as one year at the rate of as much as one cigarette or 1 gm. of tobacco a day. The number of nonsmokers in the population was estimated from the Registrar-General's figures for the number of deaths attributed to lung cancer and for the total population and from the data collected by Doll and Hill (1952) from interviews with nearly 5000 hospital patients in widely separated parts of England. Occupational hazards and the previous occurrence of certain respiratory diseases are unlikely to be of frequent etiological importance.

Polio vs. Cancer . . .

Gye (Johns Hopkins) and Syverton (Minnesota) have found that all three types of human polio virus completely destroy at least two human cancers. The polio viruses were dropped into a human cervical carcinoma that Gye has been growing in test tubes for two years and human fibrosarcoma that he has grown for fifteen years. The investigators expressed more interest in the abundant production of polio virus—which now can be

used for basic studies—than in the phenomenon of cancer's destruction. Has anyone ever tested the polio virus in cancer chemotherapy? (The virus activity in these test-tube experiments could be controlled with monkey antibodies against each type.) And has anyone ever seen statistics on the coincidence of polio infection in cancer patients?

Nodular Goiter and Thyroidectomy . . .

Sokal (Yale) poses one of the problems associated with inability to distinguish innocent from premalignant goiters. The problem confronts every surgeon who encounters an innocent nodular goiter. The problem is whether to: (1) remove the thyroid on the suspicion of its eventually becoming malignant, (2) watch it in the expectation that premalignant tumor can be detected in time for its safe removal, or (3) ignore the case on the grounds that the statistical chances of its becoming malignant are slight—or that the metastatic die already may be cast and surgery would not help. Goiter prevalence varies geographically—high in some centers like Chicago and low in areas abundant in iodine-containing foods and water. One authority states that evidence of cancer is found in about 20 per cent of single nontoxic nodules surgically removed. On the other hand, there is an indication in surgical statistics that fewer than 1 per cent of unselected nodular goiters are malignant. Thyroid cancer constitutes, roughly, about 0.5 per cent of all cancers. One set of figures showed the finding of one thyroid cancer in every 1200 autopsies—but not all thyroid cancers were the cause of death. Sources contend that many thyroid cancers, including some that are the actual cause of death, are unrecognized and unmentioned in statistical studies. The difference in estimates offered by those who argue that statistics exaggerate the incidence and prevalence of thyroid cancer and by those who say statistics underestimate the situation is not great. But the surgeon's need to make a decision—sometimes difficult—remains.

But that is not all. Shapiro has found that testosterone, injected into mice, reduced appreciably the tumor content of B, and the transaminase it activates. Thus, by giving the animals testosterone, the tumor's shortages were accentuated a great deal. Testosterone alone, however, had no direct effect in inhibiting tumor growth. But, when the testosterone was followed by a small dose of 8-azaguanine, tumor volume was reduced by one half. Similar results were obtained with flavotin (which antagonizes tumor xanthine-oxidase activity) and with 8-azaguanine.

Because of the variability of tumors--there frequently is but a faint enzymatic similarity between tumors of the same site--ideal chemotherapy along the lines suggested by Shapiro's studies should be tailor-made for each tumor. Pathological specimens would have to be analyzed chemically to determine their metabolic deficiencies. With those deficiencies defined, the patient could then be treated with a combination of analogues and potentiating compounds to increase the effectiveness of the analogues.

The results in human trials in a few centers encourage one to believe that "combination therapy" already has been launched clinically. One great drawback is the lack of precise methods of evaluating the clinical results of any treatment--conventional or experimental. Patients cannot be paired as inbred strains of mice are. A small tumor in one human frequently turns out to be much more malignant than an enormous tumor of the same site in another patient. Nevertheless, some results seem to deserve more than skeptical appraisal. The treatment of twenty-three patients with stage-3 and -4 cervical cancer (with an estimated less than 5 per cent chance for cure by any conventional means) by Klopp and others (George Washington Univ.) is well worth following. Eleven of them completed treatment with a combination of aureomycin and radiation. Six of them are alive and without evidence of the disease from four to nineteen months after treatment. Others improved. Other combinations are being tested with interesting results.

The Gordon Conference last summer heard several remarkable papers. Particularly spectacular were those by Briggs and King (Institute for Cancer Research, Philadelphia) and Kopac (New York Univ.)

Briggs demonstrated techniques that enable him to remove the nucleus from one cell and implant the nucleus of

another. The work is showing nuclear:cytoplasmic relationships and responsibilities. Nuclei from fairly well-developed embryos have been implanted in nucleus-less frog eggs, which then were fertilized and made to develop into normal embryos.

Kopac, with even smaller cells suspended in a hanging drop, removes the cytoplasm from a cell and substitutes for it cytoplasmic and other fractions extracted from other cells.

Perhaps a word of praise should be said for the cells, too, that often survive this punishment and faithfully render important biological data.

On Giving up Smoking

If afflicted with an inferiority complex, don't bother to consult a psychiatrist. Just give up smoking. When, as and if successful, and providing you are not taken away in a strait-jacket, your ego will start popping buttons all over the place. You will, in the initial stages at least, fancy yourself a granite-jawed character of indomitable will and begin to look with disdain, or pity, on all weaker mortals.

We accomplished the feat a couple of months ago and were pretty difficult to live with for a while. Our friends now give us a wide berth, but at first it was fun. It was the only way we could think of to become a man of distinction, lacking the orthodox attributes. We even found our wife referring to us with pride and renewed respect. She was apparently amazed to discover that we had it in us.

Actually we deserve little credit. Although we had tried several times before (with the usual anguish of spirit and humiliating failure), this time it was easy. The cigarette advertising did it. Never before has an industry spent so much money trying to talk itself out of business. Every hour on the half hour we are reminded that tobacco contains tars, resins, and other bronchial abrasions. Smokers are quite obviously committing slow suicide, but each brand claims that it is somewhat *less lethal* than other brands.

Any day now we expect to hear or see statements such as these: Scientific tests show that Old Dromedaries poison you more slowly than brands A, B, & D. X number of people smoked Dunhills for 30 days and lived to tell about it. Stenchies may make you cough, but so does mustard gas. Ashes to ashes, dust to dust, you know.

Out of the depth of our experience, we have come to the conclusion that the worst thing about smoking is the uncertainty. There is absolutely no assurance that it will do for you what it has done for others. According to competent medical authorities, you can get faster, surer results with one good whiff of cyanide gas or sulphur dioxide. Why drag things out?

Leggett, H. A. (Vice-President—Valley National Bank, Phoenix, Arizona). *Arizona Progress*, February, 1953; p. 1.

COMING MEDICAL MEETINGS

Date 1954	Association	City	Place
April 5-9	American College of Physicians	Chicago	
April 9-12	American Association for Cancer Research	Atlantic City	
April 12-16	American Society for Experimental Pathology	Atlantic City	
April 24-30	Industrial Medical Association	Chicago	
April 26- May 2	International Congress of International College of Surgeons	São Paulo, Brazil	
May 3-5	American Association for Thoracic Surgery	Montreal	
May 3-5	American Society of Clinical Investigation	Atlantic City	
May 17-19	American College of Surgeons (Sectional)	London	
May 20-22	American Gynecological Society	Hot Springs, Va.	
May 31- June 3	American Urological Association	New York City	Waldorf-Astoria
June 2-5	American Proctologic Association	Los Angeles	
June 17-20	American College of Chest Physicians	San Francisco	
June 18-22	Canadian Medical Association	Vancouver, B. C.	
June 21-25	American Medical Association	San Francisco	
July 23-29	Sixth International Cancer Conference	São Paulo, Brazil	
July 26-29	International Congress of Obstetrics and Gynecology	Geneva	
Aug. 9-13	National Medical Association	Washington	
Aug. 14-21	International Congress on Mental Health	Toronto, Ontario	University of Toronto
Sept. 2-9	International Society of Cell Biology	Serster, Netherlands	
Sept. 6-10	International Congress of Geographic Pathology	Washington	
Sept. 7-10	International College of Surgeons	Chicago	
Sept. 12-14	New Hampshire Medical Society	Bretton Woods	
Sept. 12-14	Vermont Medical Society	Bretton Woods	
Nov. 30- Dec. 3	American Medical Association, Clinical Session	Miami	

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